



AN ANALYSIS OF PROGNOSTIC STAGING
FOR LUNG CANCER: A NEW LOOK

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1983

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FOR LUNG CANCER: A NEW LOOK

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B.S., University of Michigan, 1979

A Thesis

Submitted to the

Department of Medicine


in Partial Fulfillment of the

Requirements for the Degree of

Doctor of Medicine

Yale University School of Medicine

1983



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ACKNOWLEDGEMENTS

I would first like to express my appreciation for my thesis advisor Dr. Alvan R. Feinstein. His willingness to venture his time and resources has been heartening. His example as a scholar, clinician, and humanitarian have been inspirational. The superlatives cannot do justice, but the special concern shown to me has not gone unnoticed. I am grateful.

I wish to offer special thanks to Carolyn Wells for her unsurpassed effort and devotion to this research. Her unflagging enthusiasm and her guidance through all aspects of the project were crucial.

The entire staff of Dr. Feinstein deserves note for their cheerful assistance. Mary Newbury deserves particular recognition for her typing assistance that kept me on schedule.

I would also like to acknowledge those who provided access to records and assistance in retrieving data, particularly the Tumor Registry at the Yale-New Haven Hospital , as well as the Medical Records Departments at the Y-NHH and the West Haven VA Hospital , and the Radiation Therapy Department at the Y-NHH.

Lastly, I would like to dedicate this thesis to my entire family, especially my father. These rare opportunities to express my love and gratitude, for all I have been given, shall not pass unheeded.

ABSTRACT

Although conventional systems of staging for patients with lung cancer rely almost exclusively on anatomic evidence, a symptomatic staging system proposed by Feinstein was able to demonstrate distinctive prognostic gradients independent of anatomic stages. Because the symptomatic staging system, however, was developed for patients with lung cancer treated during 1953-64, the current impact of the system was uncertain. The current study was planned to evaluate the prognostic role of clinical and morphologic staging features in "modern" circumstances. The analysis contains results for 131 lung cancer patients treated during 1977 in the era of improved anatomic imaging with radionuclide scans and computerized tomography.

The results contain evidence to support the three main conclusions:

1. Despite modern improvements in morphologic information, the symptomatic stages continue to produce distinctive prognostic gradients within each morphologic stage.
2. Though differences in descriptive attributes exist between the patient populations of 1953-64 and 1977, the modern patients are found and treated in stages that are symptomatically and morphologically less severe and with shorter durations of symptoms than patients in the older era, suggesting a zero-time shift.
3. The new diagnostic techniques afforded "modern" patients provide an improved accuracy of morphologic staging, which can lead to apparent improvements in the prognosis of individual stages without affecting overall survival.

INTRODUCTION

The purpose of this study was to evaluate the prognostic efficacy of a new staging system for patients with lung cancer. The new system, which had originally been developed and tested in a cohort of patients observed during 1953-64, adds a series of clinical variables to the customary morphologic information used in cancer staging. Because of modern improvements in imaging and methods for acquiring other morphologic data, the aim of this study was to determine whether survival rates for lung cancer have changed in patients with similar stages, and, if so, to appraise the contribution of new staging procedures to those changes.

The study of prognostic staging for lung cancer is important because lung cancer is the leading cause of cancer-related deaths in men¹, and appears to be reaching a similar stature among women². It has been estimated that lung cancer will develop in 135,000 Americans during 1983, and that 117,000 will die from the disease during the year¹. To use scientific methods to investigate the problems of treating lung cancer, a systematic approach is needed, beginning with a standardized assessment of the disease.

Scientific assessments must fulfill at least three basic principles³:

1. The materials prepared for the investigation and the methods of preparation must be clearly specified.

2. The instruments for evaluating critical variables must be standardized for consistency and accuracy.

3. The experimental material must be divided in a manner producing similar groups for comparison.

All three principles are essential to making results reproducible. The third principle, in particular, enables a valid assessment of the investigated therapy. If the division produced groups that varied in their susceptibility to the target event, then differences in outcome between the groups may be spuriously attributed to the treatment rather than this baseline inequality.

Baseline inequality, sometimes called susceptibility bias, can be introduced to human investigation at any of the many places where people are transferred from the general population to the therapeutic groups under comparison⁴. Prognostic analysis allows accomodation of baseline differences in outcome susceptibility, provided that the analysis contains a taxonomy for cogent prognostic features⁵. One method of prognostic analysis is to compare identical strata which are created within each total group by differences in prognostic expectations. Division of the cohort by random allocation alone cannot always assure equal proportions of these strata⁶. Providing prognostically homogeneous strata for comparison, in order to fulfill the principle of division into similar groups, requires diligent attention to differences in susceptibility.

The benefits of attention to differences in susceptibility through prognostic analysis include enabling valid assessment of

therapeutic interventions and facilitating the dissemination of scientific discoveries by helping to standardize experimental design⁷. This attention to differences in susceptibility also provides direct benefit to individual patients by more accurate quantification of prognosis and appropriate selection of therapy.

The success of prognostic analysis, which usually appears as staging systems in studies of cancer, depends on the extent to which all cogent prognostic variables are accounted for⁴. The controversy about staging systems for human cancer arises in identifying appropriate prognostic features and in classifying their relative importance.

The most common staging method for lung cancer in the United States is an adaptation of the TNM system⁸ formulated by the American Joint Committee for Cancer Staging and End-Results Reporting⁹. In this system, the anatomic extent of the disease is categorized through morphologic descriptions of the primary tumor (T), regional lymph nodes (N), and distant metastases (M). The taxonomy provides criteria for categorizing the cancer, and attempts to standardize consistency and accuracy in observing stipulated variables. The composite stages of I, II, and III are formed from the T, N, and M categories and have demonstrated a capacity to produce distinctive prognostic gradients, thus improving the homogeneity of prognostic classification^{10,11}. When applied before or after therapy, the TNM staging system enhances the valid assessment of therapeutic interventions by comparing treatments in strata with relatively similar prognoses.

Despite these advantages, the TNM system and similar morphologic staging systems do not account for all cogent prognostic variables¹². In particular, the TNM system does not deal with the biologic character of the tumor, the host, or the tumor-host interaction. Strict morphologic descriptions do not adequately account for the morbidity of tumor effects, the host susceptibility, and the biologic potential or aggressiveness of the cancer. A description of symptoms and other non-morphologic phenomena can provide valuable indices for each of these features¹³⁻¹⁶.

The primary, systemic, and metastatic features of symptoms are used to provide an indication of the functional effects of the tumor. Variations in the host susceptibility to the functional effects of tumors, or to an outcome event such as mortality, give rise to distinctly different prognostic expectations despite similar morphologic extent of disease. Demographic features may provide indirect markers for some of these variations in susceptibility. Exceptionally severe tumor effects, such as when cerebral metastases result in coma as opposed to a mild hemiparesis, would also be suspected to portend a worse prognosis. Severe co-morbidity may have prognostic significance when capable of affecting the host susceptibility, or capable of affecting the outcome event on its own. Such co-morbidity may be evident when it is deemed life-threatening, or prevents optimal diagnostic and therapeutic maneuvers. This category may include intractable cardiovascular disease and end-stage disease of other major organs.

Variations in host susceptibility result from variations in competence of host defense mechanisms. As expressed by MacDonald¹⁷ in his concept of 'biologic predeterminism', these host defense mechanisms interact with the inherent growth potential of the tumor to define the clinical course. Morphologic definitions of 'early' and 'late' stages of cancer fail to address the rate of tumor growth which represents this interaction between inherent growth potential and host defense. Symptom chronometry (i.e. the duration of symptoms before treatment), may be unable to provide information concerning change in tumor size, but can potentially provide a temporal dimension defined by the symptomatic course¹⁸. Symptomatic staging may be less valuable in this regard than in providing a taxonomy for quantifying functional effects of tumors and prognostic co-morbidity. [The term "symptomatic staging" is used to refer to a system of prognostic stratification which utilizes clinical data, consisting of symptoms and signs of disease recognized by the patient and the physician in routine bedside examination. The term "clinical staging" will be avoided because of its ambiguous application to morphologic staging systems.]

Another shortcoming of a purely morphologic staging system is that the data needed for morphologic descriptions are not always available. One type of problem is the variation in the amount of evidence that can be reasonably collected in individual patients to define the anatomic extent of the cancer. One patient may have tumor grossly visualized on a pre-therapeutic diagnostic thoracotomy, while another may have only positive sputum cytology and an ill-defined

abnormality on chest film. Advances in technology have also created problems in data availability as new techniques have been developed to increase the accuracy, thoroughness, and convenience with which a tumor's anatomic extent can be defined. For different eras in time, different amounts and types of morphologic evidence will be available to describe anatomic extent. The problem of variation in data availability is particularly relevant for diseases such as cancer, where large studies may require collections of patients spanning many years or technologic eras. The variations in the available morphologic data can be a source of bias when comparisons are based on "historical controls". This problem of variation in technologic data does not occur with symptomatic staging, since symptoms can always be identified.

The disregard for analyzing symptoms in medical research often arises from perceived deficiencies of so-called "soft data"¹⁹. Information is usually believed to be "hard" when it can be quantified on a dimensional scale, when its source can be preserved for retrospective analysis, and when it is standardized for objectivity and reproducibility. Although the "soft" decisions of clinical judgment may be considered an art, incapable of taxonomic improvements that might provide quantification and standardization, Feinstein³ has argued that this belief need not be maintained: "If the clinical judgment used in therapeutic experimentation is so scientifically defective today, it is not because the clinician's human capacities impede science, but because he has failed to use his human capacities in a scientific manner."

Since the study of clinical medicine is a study of human phenomena, the soft clinical data that are often the expression of these

phenomena play an irreplaceable role in understanding disease and its human responses. An important scientific challenge, therefore, is to find methods of hardening clinical data to improve dimensional quantification, preservation of data, and standardization, while utilizing the uniquely human qualities of soft data.

Human symptoms and signs, discerned during the bedside examination of patients, have already demonstrated a value in lung cancer assessment. Bignall²⁰ showed that prognosis in lung cancer patients varied with the duration of symptoms before diagnosis. He remarked that the morphologic definitions of "early" and "late" were misleading and that the stage of disease could be referenced by the disorder of function manifest in symptoms. Most of the work in symptomatic staging of lung cancer has been done by Feinstein^{13-16,21}, with the value of the results confirmed by others²²⁻²⁵. Symptomatic staging has also been able to produce distinctive prognostic gradients for neoplasms of the prostate^{26,27}, rectum²⁸, larynx²⁹, acute leukemia³⁰, and Hodgkin's disease³¹.

Feinstein's symptomatic staging systems for lung cancer were developed, however, for a population of patients whose lung cancers were treated during 1953-1964. Since many new technologic procedures for both diagnosis and therapy have been developed since that time, the role of symptomatic staging needs re-examination. Does the staging of symptoms still have value in the era of computerized tomography and the various radionuclide imaging techniques? The purpose of the research reported here was to answer this question. The study was intended to investigate the consistency of symptoms as "scientific

instruments", and to check their prognostic value in the assessment of contemporary patients with cancer of the lung.

MATERIALS AND METHODS

Selection of Patient Population

The inception cohort under study consists of all patients with a diagnosis of cancer of the lung and bronchus whose first anti-neoplastic therapy, or first therapeutic decision if no therapy was received, occurred at the Yale-New Haven Hospital (Y-NHH) or the West Haven Veterans Administration Hospital (WHVAH) during the calendar year of 1977. This year was chosen to allow five-year survival data to be available when the research was conducted in 1982. Eligible patients were identified through the diagnostic indices of medical records maintained at both institutions. The material of the tumor registry at the Y-NHH was also examined to check for patients treated as inpatients or outpatients at the Y-NHH during 1977.

Each appropriate medical record was solicited and evaluated for fulfillment of the following eligibility criteria: (A) the zero-time event (as defined below) must have occurred at either of the two index hospitals between January 1, 1977 and December 31, 1977; (B) the disease must have had histologic or cytologic confirmation somewhere in the clinical course, up to, and including, post-mortem; (C) the cancer must have been suspected during life.

After duplicate records were eliminated, the search yielded 340 candidate cases. Of these, 2 were eliminated because their medical record could not be located. The remaining records were reviewed in

detail and 11 were eliminated because they carried an inappropriate diagnosis. Of the remaining 327 patients, 192 were eliminated for violation of at least one of the eligibility criteria: 137 cases had a zero time outside the designated secular period; 35 cases were first treated (for the lung cancer) at a hospital other than the Y-NHH or WHVAH; 17 cases lacked microscopic evidence of cancer; and in 3 cases lung cancer was unsuspected and first discovered at necropsy. Of the remaining 135 cases, 3 were excluded because of a tissue diagnosis of carcinoid of the bronchus, leaving 132 cases available as the inception cohort for admission to this study.

Selection of Zero Time

In any study of this type, a datemark must be chosen as a temporal reference point for comparisons of clinical course. This reference point, also called zero time, was chosen as the date of the first anti-neoplastic therapy. The advantages of this date are that it is a clinically and temporally well-defined entity, even when checked in retrospect. It represents the onset of attempts to alter the clinical course, and provides a time at which all patients will be mutually comparable in their clinical course. It is also a time when the medical record tends to be most complete for clinical and paraclinical data. Details of zero time selection for patients with lung cancer³² are shown in Appendix A of the coding criteria for card 2, found in Appendix IV of this report.

Extraction of Data

The primary source of information for this survey was each patient's medical record. When necessary, supplementary data were sought

from the tumor registry files, radiation therapy files, and surgical pathology files. There were 14 cases for whom a complete medical record was not available, and for whom data were extracted solely from supplementary sources. This group consists of 7 cases extracted from tumor registry files, 4 cases from radiation therapy files, and 3 cases from abridged medical records for whom the actual record was not retrievable from storage.

The available data extracted to characterize each patient's condition were demographic, clinical, paraclinical, co-morbid, and therapeutic³². Clinical data consist of symptoms and signs of disease recognized by the patient and the physician in routine bedside questioning and examination. Paraclinical data refer to evidence of disease obtained through methods other than routine clinical examination. Such data are derived from imaging procedures, microscopic specimens, and other laboratory techniques. Co-morbid data form a complex category of information which refers to any diseases, other than lung cancer, that occur during the clinical course and that might influence either the clinical course or its interpretation.

The extraction process and the management of the occasionally imperfect data in medical records were performed according to methods presented by Feinstein, et al.³²⁻³⁴. To assure compliance with these methods, a researcher who was experienced in using them provided ongoing supervision by reviewing randomly selected extractions. An example of the extraction form used in the current study is shown in Appendix I.

Data Coding and Analysis

The extracted data were categorized and coded according to a taxonomy designed and described by Feinstein^{35,36}. Symptoms were coded as primary, systemic, or metastatic. For lung cancer, primary symptoms refer to: the bronchial symptoms of cough, hemoptysis, and subjective wheezing; the parenchymal symptoms of infection and dyspnea; and the parietal symptom of thoracic pain. Systemic symptoms refer to remote tumor effects that do not necessarily indicate dissemination of tumor beyond the lung. Such symptoms include anorexia, weight loss as a chief complaint, weakness or fatigue, and such paraneoplastic syndromes as painful hypertrophic pulmonary osteoarthropathy. Metastatic symptoms include: mediastinal symptoms, such as dysphagia, hoarseness, and superior vena caval syndrome; and symptoms indicating extrathoracic tumor extension, such as bone pain, neurologic manifestations, cutaneous masses, and symptoms of hepatic dysfunction¹³⁻¹⁵. The criteria for coding these symptoms of lung cancer can be found in the coding criteria for card 2 under columns 12-22, in Appendix IV of this report.

The coding criteria are detailed in order to minimize variability in coding symptoms. The parenchymal symptom of infection, for example, is described so as to indicate pulmonary parenchymal infections, not non-specific upper respiratory tract inflammation or extrapulmonary infection. Questions of attribution arise when a patient has a concurrent illness which produces a symptom similar to lung cancer, such as hemoptysis in a patient with active tuberculosis, or, an

infection in the contralateral lung in a patient with chronic lung disease. The coding criteria were designed to count primary and systemic symptoms as positive if there was at least questionable attribution to the lung cancer. The burden of proof in attribution of metastatic symptoms, however, was on the lung cancer. A metastatic symptom must be clearly attributable to the lung cancer to be coded as positive. For example, a patient with long-standing degenerative joint disease who complained of pain at a site of previous disease would not be coded in the metastatic clinical group. Symptoms with questionable attribution to lung cancer are discussed in depth in either column 22 or the criteria for coding the specific symptom.

The symptoms determined the classification of clinical group. The clinical groups were coded as: Asymptomatic; Long pulmonic (which included any of the primary symptoms with at least one having been present for 6 months or more, and no systemic or metastatic symptoms); Short pulmonic (primary symptoms as in long pulmonic except that all of the symptoms must have had a pre-zero time interval of less than 6 months); Systemic (must have one or more of the systemic symptoms already described and no metastatic symptoms); and Metastatic (must have at least one metastatic symptom definitely attributable to the spread of the cancer). The criteria for coding these categories can be found in Appendix C of the coding criteria for card 2, located in Appendix IV of this report.

The categories of anatomic extent of cancer were as in the TNM classification of the American Joint Committee⁹, as well as the anatomic groups: Ultrathoracic (indicating involvement outside the thorax or

involvement of an outer thoracic structure without contiguity to the chest wall); Contrathoracic (contralateral involvement within the thorax); Isothoracic (non-contiguous ipsilateral involvement within the thorax to other parenchymal structures, mediastinal structures other than lymph nodes, or any peri-thoracic structure); Vicinal (lymph nodes of the hilum or mediastinum, or any ipsilateral peri-thoracic structure, when involvement is contiguous); and Endopulmonic (none of the above). Details of coding for contiguity can be found in Appendix B of the coding criteria for card 2 and details of the anatomic groups can be found in Appendix F of the same. The coding criteria for card 2 can be found in Appendix IV of this report.

These anatomic groups were devised from morphologic evidence provided by techniques such as diagnostic imaging, bronchoscopy, mediastinoscopy, biopsy, and physical examination. This information was coded in columns 26, 27, and 29-42 of card 2. For this study, "radiographic involvement" referred to all diagnostic imaging techniques. Those techniques included the conventional roentgenographic studies as well as relatively new procedures, such as radionuclide scans and computerized tomography. Special attention was given to liver-spleen scans, brain scans, bone scans, gallium scans, Acta scan of the head, and ultrasound of the abdomen. Coding criteria for these "new techniques" can be found in the coding criteria for card 3 in columns 10-23, in Appendix V of this report.

New techniques in diagnostic imaging represent methods of defining tumor extent that were available in 1977 but not in 1953-1964.

Because new procedures to define morphologic extent of lung cancer have been developed since 1964, the data for the 1977 cohort were coded in a manner that would allow the "modern" patients to be classified in two different ways. First, according to all of the information available in 1977; and secondly, according to only the information available from procedures that could have been used in 1953-64. This classification process is described for columns 23-33 of the coding criteria for card 3, in Appendix V of this report.

The combined symptomatic-morphologic staging classification used in this study was derived from the above types of anatomic and symptomatic evidence by Feinstein and Wells³⁷. In this classification system, the final composite stages A-E are created from a combination of functional severity stages and toponymic stages. Functional severity is itself a combination of symptom severity and prognostic co-morbidity. The symptoms coded under functional severity were dyspnea, systemic symptoms, metastatic symptoms of questionable attribution, and tumor effects that were excessively severe (as defined for column 44 of the coding criteria for card 2, in Appendix IV of this report). Prognostic co-morbidity denotes a condition or associated ailment, other than the lung cancer, that is expected to have a more unfavorable effect on the outcome of the clinical course than is otherwise anticipated. This category includes intractable cardiovascular disease and end-stage disease of other major organs.

The toponymic stages were classified from a combination of morphologic and symptomatic evidence used to define the topographic

extent of the lung cancer. Toponymic stage is divided into 7 strata.

In descending order of extensiveness the strata are:

7 = Liver/Other: evidence of metastasis to deep, vital organs other than brain or bone, and beyond the thorax;

6 = All other ultrathoracic sites: evidence of metastasis to CNS, bone, or surface nodules beyond the thorax;

5 = Intrathoracic: implies massive spread within the thorax;

4 = Isothoracic: non-contiguous spread within the thorax on the same side as the primary tumor;

3 = Vicinal: spread limited to contiguous sites within the thorax;

2 = Symptomatic or Central: includes primary symptoms other than dyspnea, or central location of the tumor;

1 = Asymptomatic and Peripheral.

The coding criteria for toponymic stages, as well as functional severity stages and composite stages, are located in the coding criteria for card 3 under columns 34-36, in Appendix V of this report.

The coding criteria for therapeutic decisions are presented under columns 47-48 of the coding criteria for card 2. Criteria for further description of surgery, if performed, and of the subsequent clinical course are also present in the coding criteria for card 2. As evidenced by the coding cards and coding criteria presented in the Appendix, a large amount of information was extracted and coded but not used in the current study. The entire list of criteria, however, are appended for easy reference.

Except for the coding criteria concerning new diagnostic techniques, which were designed for this study, the coding criteria used for both cards 2 and 3 (Appendix IV and V respectively) were compiled by Dr. Feinstein and his clinimetric research group for a cohort of patients from 1953-64. The criteria were meticulously maintained; and again, an experienced researcher checked a random sample of the coded extractions to assure consistency. She also helped in decisions about difficult cases. After all of the extractions were coded and the coding problems addressed, each of the extractions was re-checked, blinded to the outcome event, to assure consistency in coding. Examples of the coding cards can be located in Appendix II (card 2) and Appendix III (card 3).

Once coded, the data were keypunched onto Hollerith cards and the punched cards were doubly verified. Data analysis was then performed using an IBM 4341 computer with SAS program package. Because the gradients produced by the numbers were clearly evident, tests of statistical significance have been omitted. [I am grateful to Carolyn K. Wells for assistance in checking the extractions and the coding, as well as for performing the computer procedures.]

Outcome Variable

The data collected by the described methods were analyzed for prognosis according to survival rate. Six-month survival was chosen for most of this analysis because the median survival of the cohort was close to 6 months, and because follow-up information was usually readily available at that point. The analysis was performed on 131 of the 132 cases admitted to the survey because no follow-up information was available for

one case after his zero-time admission. Nine other cases lacked follow-up data to either death or 5-year survival. They were accounted for in survival rates, for times beyond the available follow-up data, by being deleted from both the numerator and the denominator of the calculated survival rates.

Previous Cohort for Comparison

The results of the 1977 cohort were compared with those found in an analogous cohort of patients, studied with similar methods, whose zero times occurred at Yale-New Haven and West Haven VA Hospitals during the years 1953-64, and whose results have been described previously^{21,37}. The data for that "old" cohort, which were computer coded in a manner similar to the techniques employed here, were made available for the contrasts under discussion.

RESULTS

Descriptive Data

The basic descriptive data for the 1977 and 1953-1964 cohorts are provided in the first 5 tables. These data describe the similarities and the differences in the composition of the two cohorts. The differences raise intriguing questions about the epidemiology of lung cancer in modern patients. Differences in prognosis for the new cohort may result simply from the changing composition of the lung cancer patient population. If the cause of prognostic change were to be concluded from a comparison of two cohorts then the prognostic analysis must correct for the differences in baseline composition of the two cohorts. The data from the 1953-1964 cohort are presented in this report to illustrate the different zero-time characteristics of a modern population of lung cancer patients and to evaluate the role of symptomatic staging for a new, albeit different population. Since this report will not make conclusions of cause and effect derived from a comparison of the two cohorts, an analysis which corrects for differences in composition according to descriptive attributes will not be reported here.

The demographic data for the two cohorts are shown in Table 1. The gender composition of the modern cohort continues to be male dominated, but the proportion of females has increased substantially

since 1953-64. Though there is some redistribution in age category composition, the median age is similar for both patient populations. The hospital at which zero time occurred is more heavily weighted by Y-NHH in the 1977 survey. The race distribution remains predominately white, although there is an increased proportion of blacks in the new group.

Descriptive histologic data are shown in Table 2. Fewer well-differentiated neoplasms occur in the modern cohort, but the change may reflect differences in histologic criteria for pathologists. The coding criteria for histologic classification presented in this report can be found in Appendix D of the coding criteria for card 2, located in Appendix IV of this report.

Description of aspects of the diagnostic work-up which were unique to the 1977 cohort are presented in Table 3. Positive and equivocal results are defined in Appendix V under coding criteria for card 3. The category of "other" under new diagnostic techniques refers to computerized tomography used at sites other than the head and to ultrasonic imaging used outside the abdomen.

Table 4 shows the overall survival data up to 5 years. This information is also displayed in Figure 1 as survival curves. There is a notable improvement in survival rates at the various times after zero time for the new cohort up until 5 years. The median survival of the new cohort has increased more than 2 months beyond that of the 1953-64 patient population.

Descriptive data for therapy are shown in Table 5. This table describes the initial therapy regardless of whether subsequent therapy was provided. Of interest is that fewer patients received thoracotomy without excision of the primary tumor in 1977 than in 1953-64. While fewer people went without therapy of any kind in 1977, the only notably increased therapeutic maneuver was radiation therapy to the primary tumor. The use of thoracotomy and of chemotherapy as first therapy changed little. Zero-time therapy is evaluated according to six-month survival to give a sample of interesting trends. Of note is that the improvements in survival for the modern cohort have come in the traditional modes of therapy -- thoracotomy and radiation therapy -- and not in the evolving realm of chemotherapeutics. There are many potential explanations for results in this table, but the complex analysis required to draw substantial conclusions demands a larger cohort. Further appraisal of these issues in therapy will await enlargement of the patient sample.

The remaining tables introduce the principal topics of the present study. They can be considered under three headings:

1. Prognostic Effect of Symptomatic Staging
2. Zero-time Shift ("Lead-Time Bias")
3. Impact of New Technology

Prognostic Effect of Symptomatic Staging

Tables 6-8 present the 6-month survival rates for both cohorts according to symptomatic stages. The clinical groups¹³ in Table 6 represent the zero-time symptomatic state. The functional

severity stages³⁷ in Table 7 represent a combination of symptom severity and prognostic co-morbidity. The composite stages³⁷ in Table 8 represent the final staging categories resulting from a combination of morphology, symptoms, and functional severity. Survival gradients are produced by each of these symptomatic staging methods in both the 1953-64 and 1977 cohorts. The gradients between some of the stages have sharper definition in the 1953-64 cohort than in 1977.

Survival gradients for symptomatic stages can also be defined within the morphologic stages of the conventional TNM staging system. Table 9 demonstrates this striking gradient-within-gradient effect by presenting clinical group staging concomitantly with TNM staging. The clinical groups are presented as Indolent (a combination of asymptomatic and long pulmonic), Obtrusive (a combination of short pulmonic and systemic symptoms), and Deleterious (metastatic symptoms). The clinical groups were combined in this manner because the combinations were used in a previous report¹⁵ and because they increase the numbers available for statistical appraisal of each cell. As shown in Table 9, the clinical groups produce a distinct prognostic gradient within each TNM stage. Conversely, within any clinical group the TNM stages produce a distinct prognostic gradient. Table 10 contrasts the composite stages A-E with the TNM stages. This table does not show a good double gradient. TNM does not impact on the composite stages, as might be expected since the composite stages already account for morphology. The composite stages do show a prognostic gradient within TNM stages but the gradients are not sharp and many cells contain few patients.

The presence of sharper prognostic gradients using clinical features in 1953-64 versus 1977 prompts questioning of the amount that symptomatic staging benefits the new cohort relative to the old cohort. Since this report was not designed to address cause-effect comparisons between the two cohorts, the issue of the relative benefit of symptomatic staging in old versus new patient populations cannot be addressed here. However, a number of competing explanations for the less distinct prognostic gradients of the 1977 cohort can be considered:

1. baseline differences between cohorts resulting from a changing lung cancer patient population may adversely affect the efficacy of the symptomatic staging system for the 1977 cohort;
2. changes in primary or ancillary therapy may have altered survival rates of select groups of patients;
3. since the prognostic gradients of 1953-64 were observed in the cohort which generated the prognostic system, the new population could not be expected to match the "best fit" gradient and, therefore, the prognostic system appears to be less discriminating in the new population used to test it; and
4. variability in the prognostic gradients of the 1977 cohort may be attributable to the nearly 10-fold smaller sample size relative to the 1953-64 cohort.

However, the results confirm the expectation that clinical phenomena continue to show prognostic significance despite the more precise morphologic staging available in a modern cohort and despite possible baseline inequalities between cohorts. The data for symptom

types, and symptom severity, and co-morbid severity provided distinctive prognostic gradients and the gradients were maintained in the unified categories of the composite stages. That these symptomatic stages were able to show gradients within TNM stages, and vice versa, indicates that each of the two types of staging independently yields prognostic discrimination not provided by the other. Thus, the current study reiterates the importance of classifying both morphologic and symptomatic features in prognostic analysis for the evaluation of lung cancer therapy.

Zero-Time Shift

Tables 11-14 display the composition of both the 1977 and 1953-64 cohorts categorized by morphologic and symptomatic stages. Table 11 shows that the 1977 cohort contains a higher percentage of patients who are in the more favorable TNM morphologic stages at zero time. Clinical group, functional severity, and composite stage all show a shift to less severe stages in the 1977 cohort.

The shift to less severe stages is demonstrated more graphically when the composition of the 1977 cohort is examined without the results from new diagnostic techniques. By comparing the cohorts in this way, a similar standard of diagnosis can be applied to both cohorts in categorizing morphologic extent of disease. Table 15 shows the composition of both cohorts according to TNM stages constructed without the use of data from new diagnostic tests. Table 16 has a similar comparison, according to composite stages.

A final aspect that bears on cohort composition at zero time is the "progression interval" in patients who had symptoms at zero time. The progression interval refers to the length of time from inception of symptoms until zero time¹⁸. The number of symptomatic patients in the 1977 cohort was 112 (85%), and the median progression interval was 3.0 months. The 1953-64 cohort contained 1173 (93%) symptomatic patients with a median progression interval of 5.4 months.

This demonstrated shift in zero time is sometimes referred as lead time. The term is generally applied to increased survival time provided by early diagnosis as a result of screening³⁹, which enables the disease to be found at an earlier time than would have occurred with conventional clinical diagnosis. This study does not address the impact of screening, since the population of patients was not derived from a screening program. There are strong suggestions, however, that members of the 1977 cohort appeared earlier for diagnosis and treatment of their lung cancer than the 1953-64 cohort. The evidence for this zero-time shift, or lead-time bias, is demonstrated in the zero-time data of the 1977 cohort, from the smaller percentage of patients who had symptoms or were in severe morphologic or symptomatic stages, and also from the shorter progression interval for the symptomatic patients.

At zero time, 15% of the 1977 cohort was without lung cancer symptoms, in contrast to only 7% of the 1953-64 cohort. Although the results suggest at least passive improvements in screening for lung cancer since 1953-64, this study does not provide sufficient information to draw further conclusions.

The results showing a smaller percentage of patients in both severe morphologic and symptomatic stages at zero time in 1977 indicate that the improvement in the 1977 cohort is most striking when similar staging information is used for morphologic features. The lower percentage of severe clinical groups, and the notably higher percentage of the 1977 cohort lacking any functional severity, also demonstrate a clinically "earlier" composition of the modern population of patients.

The modern population of patients possesses a shorter progression interval of symptoms than the 1953-64 cohort. This smaller time interval from onset of symptoms to zero time is also suggestive of a zero-time shift. Thus, it appears that, for whatever reasons, the modern population of patients comes to therapy in a more favorable clinical state than in 1953-64.

Impact of New Technology

The "new technology" in this study consists of new techniques in diagnostic imaging that were available to the 1977 but not to the 1953-64 cohort. In particular, the new techniques include the scans of nuclear imaging, computerized tomography, and ultrasonic imaging that were used to define tumor extent. Tables 17-20 present survival rates with special attention to the results of these techniques. The survival rates are reported for stages assigned by using three categories of data: (1) information that excludes results from the new techniques, i.e. the "old" results; (2) information that includes unequivocal results of new techniques; or, (3) information that includes both

unequivocal and equivocal results counted as "positive". The data reported earlier for the 1977 cohort includes only unequivocal results unless otherwise specified. Although equivocal results are often used in staging³⁸, they are displayed separately for clarity.

Table 17 shows the 6-month survival rates according to TNM stages for the three categories of data. It portrays a striking improvement in prognosis for each stage as the data are expanded from the "old" information, to include first the unequivocal and later the equivocal results of new techniques. These improvements in prognosis for each stage occur simply as acts of staging, without altering the cohort itself, or the overall survival rates in the cohort. Table 18 shows the same for composite stages, and Table 19 and 20 show 5-year survival rates for TNM and composite stages respectively.

DISCUSSION

This study was concerned neither with the etiology of lung cancer nor with the results of its primary or ancillary therapy. The goal was to examine the methods that can be used for the prognostic assessment of lung cancer. Not all of the data acquired in the research were analyzed in this report. Some information will be used in future reports and other analyses await the enlarged numbers of an expanded cohort.

The three major topics addressed in this report are: the impact of clinical phenomena on lung cancer staging; the effect of a zero-time shift between 1953-64 and 1977; and the impact of new diagnostic techniques on the staging of lung cancer. Since the first two topics were discussed when the results were presented, the rest of this discussion

will focus on the impact of improved diagnostic methods on the staging of lung cancer.

The 1977 cohort investigated in this study has been contrasted with a cohort whose cancers occurred at least 12 years earlier, during 1953-64. When contrasted with a newer population of patients, previous patients deemed to have the same clinical condition but managed differently are called "historical controls". "Historical controls" are often used to assess new treatment when comparisons with "concurrent controls" are unfeasible for ethical, financial, or logistical reasons. The major hazards of comparison with historical controls are the biases produced by unrecognized differences in pre-treatment clinical condition and by differences in ancillary therapy.

Since new technology provides new standards of care in diagnosis and therapy, secular changes can occur in both baseline assessment and ancillary therapy. The observed improvement in survival rates for the 1977 cohort versus the 1953-64 cohort may be attributable to improvements in therapy, to the "zero-time shift", or to baseline inequality between cohorts arising from the changing composition of the lung cancer cohort. A different source of improvement in survival rates, however, has been strikingly demonstrated in the third part of this study. Major improvements have occurred simply from changes in staging created by advances in diagnostic technology.

While the data extraction was in progress during the research, it became apparent that the morphologic extent of lung cancer for patients in 1977 was defined with data that were not available for patients in

the earlier cohort. The new diagnostic techniques were particularly useful in demonstrating symptomless metastatic disease or in providing morphologic confirmation of symptomatic metastases. The improving capacity to identify metastatic disease would allow many patients who would previously have been classified without this evidence, to receive a "proper" categorization as metastatic.

Mintz, et al.⁴⁰, using many of the same new imaging techniques examined in the current study, were able to demonstrate an increased capacity to detect otherwise unrecognized spread of lung cancer. The routine use of liver-spleen scans, bone scans, CT scans of the brain, and total-body gallium scans created significant changes in the TNM stage composition of the group when compared with the initial staging without these techniques. Similar results have been demonstrated using CT scans of the abdomen and thorax.⁴¹

The cited studies, however, have not addressed the altered prognosis produced by changing the composition of pre-therapeutic stages. The current research demonstrates that prognosis itself, regardless of therapeutic effects, is improved by the contributions of the new diagnostic technology.

Since increased morphologic extensiveness of lung cancer has been shown to portend a worse prognosis, a patient who had asymptomatic metastases that went undetected during pre-therapeutic staging would be expected to lower the overall survival of the "higher" stage to which he was originally assigned. Having fewer symptomatic manifestations of the disease, however, such a patient may have a better prognosis than

the other patients in the "lower" stage, to which he is assigned when better data are available. Because of the accurate staging, survival rates can be improved for the stage that the patient leaves and also for the stage that he joins. Nevertheless, prognosis will have changed for neither the individual nor the total cohort.

This migratory shift, which seems to produce major changes in the surroundings without any changes in the shifted entity, is analogous to a phenomenon described in a quotation attributed to Will Rogers: "When the Okies left Oklahoma and moved to California, they raised the average IQ of both states". A graphic demonstration of this "Will Rogers Phenomenon" is provided in the survival rates found for the 1977 cohort, staged with and without the application of new diagnostic techniques. Since the members of the cohort are being compared with themselves, nothing can change for the individual people or for the total survival rate in the cohort. Nevertheless, with the data from the new technology, the survival rate improves for each stage!

The "Will Rogers Phenomenon" has important implications when the results of new treatments for cancer are compared with survival rates found in "historical controls". The new treatments may seem impressively better, but the superiority may arise from diagnostic rather than therapeutic improvements. An attention to all prognostic variables, rather than morphologic data alone, can help prevent this error and can improve the validity of therapeutic assessments.

Thus, the results of this study have three main conclusions:

1. The symptoms produced by lung cancer are still important,

although generally ignored variables for estimating prognosis and evaluating therapy in a modern population of patients.

2. A shift in zero time has occurred for modern patients with lung cancer, whereby the patients receive treatment while in more favorable stages, and may contribute to the improved survival in the total cohort.

3. Some (or much) of the improved survival in the morphologic stages of modern patients may be attributable to improvements in diagnostic technology, which can alter the staging classification of patients without truly affecting the results in the individuals or in the total group.

Figure 1. SURVIVAL CURVES FOR THE TWO COHORTS

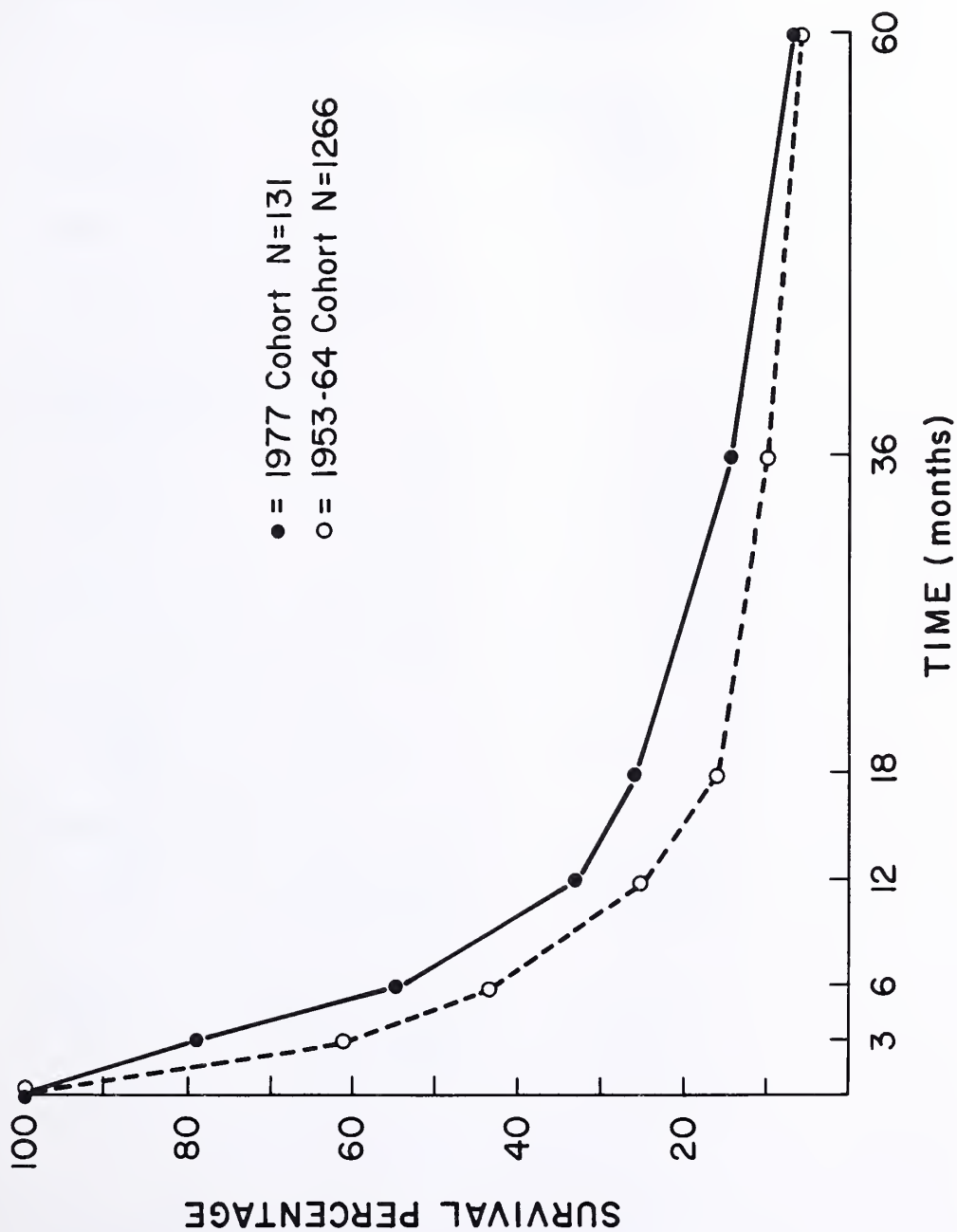


Table 1. COMPOSITION OF THE TWO COHORTS
ACCORDING TO DEMOGRAPHIC ATTRIBUTES

Demographic Attribute	Cohort	
	1977 N = 131	1953-64 N = 1266
<u>Gender</u>		
Men	96 (73%)	1118 (88%)
Women	35 (27%)	148 (12%)
<u>Age (years)</u>		
<40	4 (3%)	34 (3%)
40 - 49	8 (6%)	134 (11%)
50 - 59	37 (28%)	330 (26%)
60 - 69	42 (32%)	527 (42%)
70 - 79	33 (25%)	222 (18%)
>79	7 (5%)	19 (2%)
Median	63	63
Range	34 - 83	25 - 91
<u>Hospital</u>		
Y-NHH	99 (76%)	867 (68%)
WHVAH	32 (24%)	399 (32%)
<u>Race</u>		
White	119 (91%)	*556 (96%)
Black	12 (9%)	24 (4%)
Oriental	--	2 (<1%)

*Race composition for the 1953-64 cohort was available only for patients seen during 1960-64. N = 582

Note: Total proportions in composition of a cohort may not sum to 100% in this and subsequent tables, because of "rounding errors".

Table 2. COMPOSITION OF THE TWO COHORTS ACCORDING
TO HISTOLOGIC CLASSIFICATION

<u>Histologic Classification</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953-64</u>
Well-Differentiated Epidermoid	21 (16%)	338 (27%)
Well-Differentiated Adenocarcinoma	26 (20%)	227 (18%)
Small Cell	9 (7%)	109 (9%)
Anaplastic	60 (46%)	418 (33%)
Metastatic	1 (1%)	15 (1%)
Cytology Only	14 (11%)	159 (13%)
TOTAL	131 (100%)	1266 (100%)

Table 3. FREQUENCY OF PERFORMANCE AND RESULTS OF NEW DIAGNOSTIC
TECHNIQUES EMPLOYED IN THE 1977 COHORT

<u>Study</u>	N = 132 <u>Performed</u>	<u>Result</u>	
		<u>Positive</u>	<u>Equivocal</u>
Liver-Spleen Scan	98 (74%)	10/98 (10%)	6/98 (6%)
Brain Scan	79 (60%)	8/79 (10%)	4/79 (5%)
Bone Scan	73 (55%)	12/73 (16%)	17/73 (23%)
Head Acta Scan	12 (9%)	7/12 (58%)	0/12 (0%)
Abdominal Ultrasound	14 (11%)	2/14 (14%)	5/14 (36%)
Gallium Scan	32 (24%)	10/32 (31%)	10/32 (31%)
Other	9 (7%)	5/9 (56%)	1/9 (11%)

* "Other" was coded when a study performed to define tumor extent was not available during the 1953-64 survey, and is not listed above. In this study, the category was used for CT other than head, and for ultrasound outside the abdomen.

Table 4. SURVIVAL RATES FOR THE TWO COHORTS
AT VARIOUS TIMES AFTER ZERO TIME

Time Since Zero Time	Cohort	
	1977 N = 131	1953-64 N = 1266
3 Months	103/131 (79%)	776 (61%)
6 Months	72/131 (55%)	551 (44%)
12 Months	44/130 (34%)	324 (26%)
18 Months	35/130 (27%)	220 (17%)
36 Months	20/128 (16%)	128 (10%)
60 Months	10/122 (8%)	86 (7%)

Median Survival (Mos.)	6.65	4.60

* For the 1953-64 cohort, survival information is available for all 1266 patients. For the 1977 cohort, certain patients seemed to be "lost to follow-up" when this research was done. The changing denominators in the 1977 survival rates reflect these losses.

Table 5. DISTRIBUTION AND SIX-MONTH SURVIVAL RATES FOR THE TWO COHORTS ACCORDING TO THE FIRST COURSE OF THERAPY

First Course of Therapy	Cohort		6 Month Survival	
	1977	1953 - 64	1977	1953 - 64
Thoracotomy With Excision of Primary	35 (27%)	324 (26%)	35/35 (100%)	251/324 (77%)
Thoracotomy Without Excision of Primary	6 (5%)	108 (9%)	4/6 (67%)	60/108 (56%)
Radiation Therapy to Primary	52 (40%)	413 (33%)	25/52 (48%)	160/413 (39%)
"Cytotoxic" Therapy	7 (5%)	91 (7%)	1/7 (14%)	14/91 (15%)
Radiation and Cytotoxic	11 (8%)	36 (3%)	3/11 (27%)	11/36 (31%)
Metastatic Therapy Alone	11 (8%)	97 (8%)	2/11 (18%)	27/97 (28%)
No Therapy	9 (7%)	197 (16%)	2/9 (22%)	28/197 (14%)
TOTAL	131 (100%)	1266 (100%)	72/131 (55%)	551/1266 (44%)

Table 6. SIX-MONTH SURVIVAL RATES FOR THE TWO COHORTS
ACCORDING TO CLINICAL GROUPS

<u>Clinical Group</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953 - 64</u>
Asymptomatic	14/19 (74%)	68/88 (77%)
Long Pulmonic	13/17 (76%)	91/148 (61%)
Short Pulmonic	28/44 (64%)	107/193 (55%)
Systemic	11/22 (50%)	175/417 (42%)
Metastatic	6/29 (21%)	110/420 (26%)
TOTAL	72/131 (55%)	551/1266 (44%)

Table 7. SIX-MONTH SURVIVAL RATES FOR THE TWO COHORTS
ACCORDING TO FUNCTIONAL SEVERITY STAGES

<u>Functional Severity</u>	<u>1977</u>	<u>1953-64</u>
None	45/72 (63%)	218/340 (64%)
Systemic/Dyspnea	22/36 (61%)	281/607 (46%)
Quasi-Metastatic	1/3 (33%)	32/94 (34%)
Severe	4/20 (20%)	20/225 (9%)
TOTAL	72/131 (55%)	551/1266 (44%)

Table 8. SIX-MONTH SURVIVAL RATES FOR THE TWO COHORTS
 ACCORDING TO COMPOSITE STAGES

<u>Composite Stage</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953-64</u>
A	23/24 (96%)	116/133 (87%)
B	32/39 (82%)	253/393 (64%)
C	12/38 (32%)	147/415 (35%)
D	5/24 (21%)	33/238 (14%)
E	0/6 (0%)	2/87 (2%)
TOTAL	72/131 (55%)	551/1266 (44%)

Table 9. SIX-MONTH SURVIVAL RATES FOR THE 1977 COHORT
PRESENTED BY CLINICAL GROUPS AND
TNM STAGES CONCOMITANTLY

<u>Clinical Group</u>	<u>TNM Stage</u>			<u>TOTAL</u>
	<u>I</u>	<u>II</u>	<u>III</u>	
Indolent	12/13 (92%)	8/10 (80%)	7/13 (54%)	27/36 (75%)
Obtrusive	18/21 (86%)	9/13 (69%)	12/32 (38%)	39/66 (59%)
Deleterious	--	--	6/29 (21%)	6/29 (21%)
TOTAL	30/34 (88%)	17/23 (74%)	25/74 (34%)	72/131 (55%)

Table 10. SIX-MONTH SURVIVAL RATES FOR THE 1977 COHORT
PRESENTED BY COMPOSITE AND TNM STAGES CONCOMITANTLY

<u>Composite Stage</u>	<u>TNM Stage</u>			<u>TOTAL</u>
	<u>I</u>	<u>II</u>	<u>III</u>	
A	22/23 (96%)	1/1 (100%)	--	23/24 (96%)
B	8/9 (89%)	10/14 (71%)	14/16 (88%)	32/39 (82%)
C	0/1 (0%)	2/3 (67%)	10/34 (29%)	12/38 (32%)
D	0/1 (0%)	4/5 (80%)	1/18 (6%)	5/24 (24%)
E	--	--	0/6 (0%)	0/6 (0%)
TOTAL	30/34 (88%)	17/23 (74%)	25/74 (34%)	72/131 (55%)

Table 11. COMPOSITION OF THE TWO COHORTS
ACCORDING TO TNM STAGES

<u>TNM Stage</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953-64</u>
I	34 (26%)	281 (22%)
II	23 (18%)	172 (14%)
III	74 (56%)	813 (64%)
TOTAL	131 (100%)	1266 (100%)

Table 12. COMPOSITION OF THE TWO COHORTS
ACCORDING TO CLINICAL GROUPS

<u>Clinical Group</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953-64</u>
Asymptomatic	19 (15%)	88 (7%)
Long Pulmonic	17 (13%)	148 (12%)
Short Pulmonic	44 (34%)	193 (15%)
Systemic	22 (17%)	417 (33%)
Metastatic	29 (22%)	420 (33%)
TOTAL	131 (100%)	1266 (100%)

Table 13. COMPOSITION OF THE TWO COHORTS
ACCORDING TO FUNCTIONAL SEVERITY STAGES

<u>Functional Severity</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953-64</u>
None	72 (55%)	340 (27%)
Systemic/Dyspnea	36 (27%)	607 (48%)
Quasi-Metastatic	3 (2%)	94 (7%)
Severe	20 (15%)	225 (18%)
TOTAL	131 (100%)	1266 (100%)

Table 14. COMPOSITION OF THE TWO COHORTS
ACCORDING TO COMPOSITE STAGES

<u>Composite Stage</u>	<u>Cohort</u>	
	<u>1977</u>	<u>1953-64</u>
A	24 (18%)	133 (11%)
B	39 (30%)	393 (31%)
C	38 (29%)	415 (33%)
D	24 (18%)	238 (19%)
E	6 (5%)	87 (7%)
TOTAL	131 (100%)	1266 (100%)

Table 15. COMPOSITION OF THE TWO COHORTS
ACCORDING TO TNM STAGES WITHOUT DATA
FROM NEW DIAGNOSTIC TECHNIQUES

TNM Stage "Old" Morphologic Data Only	Cohort	
	1977	1953-64
I	42 (32%)	281 (22%)
II	25 (19%)	172 (14%)
III	64 (49%)	813 (64%)
TOTAL	131 (100%)	1266 (100%)

Table 16. COMPOSITION OF THE TWO COHORTS
ACCORDING TO COMPOSITE STAGES WITHOUT
DATA FROM NEW DIAGNOSTIC TECHNIQUES

Composite Stage "Old" Morphologic Data Only	Cohort	
	1977	1953-64
A	26 (20%)	133 (11%)
B	45 (34%)	393 (31%)
C	37 (28%)	415 (33%)
D	21 (16%)	238 (19%)
E	2 (2%)	87 (7%)
TOTAL	131 (100%)	1266 (100%)

Table 17. SIX-MONTH SURVIVAL RATES FOR THE 1977 COHORT
PRESENTED FOR TNM STAGES DETERMINED WITH INCREASING
AMOUNTS OF INFORMATION FROM NEW DIAGNOSTIC TECHNIQUES

TNM Stage	Information Used In Staging		
	<u>"Old"</u> <u>Technologic</u> <u>Data Only</u>	<u>All Technologic</u> <u>Data, With Only</u> <u>Unequivocal Results</u> <u>Counted As Positive</u>	<u>All Technologic</u> <u>Data, With</u> <u>Equivocal Results</u> <u>Counted As Positive</u>
I	32/42 (76%)	30/34 (88%)	22/24 (92%)
II	17/25 (68%)	17/23 (74%)	14/19 (74%)
III	23/64 (36%)	25/74 (34%)	36/88 (41%)
TOTAL	72/131 (55%)	72/131 (55%)	72/131 (55%)

Table 18. SIX-MONTH SURVIVAL RATES FOR THE 1977 COHORT
PRESENTED FOR COMPOSITE STAGES DETERMINED WITH INCREASING
AMOUNTS OF INFORMATION FROM NEW DIAGNOSTIC TECHNIQUES

<u>Composite Stage</u>	<u>Information Used In Staging</u>		
	<u>"Old"</u> <u>Technologic</u> <u>Data Only</u>	<u>All Technologic</u> <u>Data, With Only</u> <u>Unequivocal Results</u> <u>Counted As Positive</u>	<u>All Technologic</u> <u>Data, With</u> <u>Equivocal Results</u> <u>Counted As Positive</u>
A	23/26 (88%)	23/24 (96%)	18/19 (95%)
B	34/45 (76%)	32/39 (82%)	24/28 (86%)
C	11/37 (30%)	12/38 (32%)	20/43 (47%)
D	4/21 (19%)	5/24 (21%)	10/35 (29%)
E	0/2 (0%)	0/6 (0%)	0/6 (0%)
TOTAL	72/131 (55%)	72/131 (55%)	72/131 (55%)

Table 19. FIVE-YEAR SURVIVAL RATES FOR THE 1977 COHORT
PRESENTED FOR TNM STAGES DETERMINED WITH INCREASING
AMOUNTS OF INFORMATION FROM NEW DIAGNOSTIC TECHNIQUES

<u>TNM Stage</u>	<u>Information Used In Staging</u>		
	<u>"Old"</u> <u>Technologic</u> <u>Data Only</u>	<u>All Technologic</u> <u>Data, With Only</u> <u>Unequivocal Results</u> <u>Counted As Positive</u>	<u>All Technologic</u> <u>Data, With</u> <u>Equivocal Results</u> <u>Counted As Positive</u>
I	7/35 (20%)	7/28 (25%)	6/19 (32%)
II	2/23 (9%)	2/21 (10%)	2/17 (12%)
III	1/64 (2%)	1/73 (1%)	2/86 (2%)
TOTAL	10/122 (8%)	10/122 (8%)	10/122 (8%)

Table 20.

FIVE-YEAR SURVIVAL RATES FOR THE 1977 COHORT
PRESENTED FOR COMPOSITE STAGES DETERMINED WITH INCREASING
AMOUNTS OF INFORMATION FROM NEW DIAGNOSTIC TECHNIQUES

<u>Composite Stage</u>	<u>Information Used In Staging</u>		
	<u>"Old"</u> <u>Technologic</u> <u>Data Only</u>	<u>All Technologic</u> <u>Data, With Only</u> <u>Unequivocal Results</u> <u>Counted As Positive</u>	<u>All Technologic</u> <u>Data, With</u> <u>Equivocal Results</u> <u>Counted As Positive</u>
A	6/21 (29%)	6/19 (32%)	5/15 (33%)
B	4/43 (9%)	4/37 (11%)	4/26 (15%)
C	0/36 (0%)	0/37 (0%)	1/41 (2%)
D	0/20 (0%)	0/23 (0%)	0/34 (0%)
E	0/2 (0%)	0/6 (0%)	0/6 (0%)
TOTAL	10/122 (8%)	10/122 (8%)	10/122 (8%)

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APPENDICES

Appendix I: Extraction Form

Appendix II: Coding Card 2

Appendix III: Coding Card 3

Appendix IV: Coding Criteria Card No. 2

Appendix V: Coding Criteria Card No. 3

Form Complete ☐
 Extractor
 Checker

.....
 Patient Coding
 Number

LUNG CANCER EXTRACTION FORM

6. NECROPSY No. Hosp. NONE
 UNK

Cell Type: NO TUMOR
 POUND

LUNG:

EXTRATHORACIC STRUCTURES:

Liver:

Brain:

Adrenals:

THORACIC STRUCTURES:

REMARKS:

1. MEDICAL ITINERARY

INDEX HOSP.

Unit No. Date Date
 Adm: Disch:

ZERO TIME HOSP.

Unit No. Date Date
 Adm: Disch:

REF HOSPS: Date Date
 Adm: Disch:

REASON(S) FOR TRANSFER(S):

2. DEMOGRAPHIC DATA

D.O.B. Age Race
 M F
 Sex

7. INTERVALS

Date of Death:

Source: Date Last Alive:

★ to ADM: ★ to ZT:

→ to ADM: → to ZT:

ADM to ZT: ZT to END:

8. SPECIAL COMMENTS

OTHER SOURCES TO CHECK				DONE

SMOKING HISTORY:
 CUSTOMARY CIGARETTES:

CHANGE IN SMOKING HABITS:

Unk. H Smoked Amt. Unk.
 0 1/2 1/2 to 1
 1 1 to 2 2

Years:
 PIPE, CIGAR OR OTHER TOBACCO HABIT:

3. ZERO STATE DATA

PRESENT ILLNESS

SYMPTOMS AND SUBJECTIVE SIGNS

ASYMPTOMATIC

COUGH Non Prod
Prod

HEMOPTYSIS

SUBJECTIVE WHEEZE

INFECTION Flu Chills
Cold Fever Single
URI Sweets Recurrent
Clin Dx Pn Unresolved Pn

DYSPNEA

THORACIC PI Non PI Unk
ACHE OR PAIN Location:

ANOREXIA

WEAKNESS
FATIGUE
SIGNIFICANT MALAISE

WT. LOSS Chief Complaint
Symptom

CLUBBING (Noted by Pt.)

JOINT PAIN

HOARSENESS: NMVC NEVC MVC

SWELLING OF: Face Arm Neck

DYSPHAGIA

PALPABLE MASS (Noted by Pt.)

NEUROLOGIC SX:

OTHER SX:

PERTINENT SIGNS AND SYNDROMES NOTED BY M.D.

PARACLINICAL DATA

RADIOGRAPHIC DATA

Reg Lem Met S. Angio B'gram

R APEX L APEX
RUL LUL
RUF LUF
RAL LAL
RLF LLF
RLF

Hilum
Mediast.
R Pleura
Pl. Eff.
L Rib
Chest Wall
Diaphragm

BONE(S):

LATEST NEG:

EARLIEST EQUIV:

OTHER STRUCTURE(S):

EARLIEST POS:

BRONCHOSCOPY

Not Done Neg. No Mass

TRACHEA
CARINA
RAB
RULB
RALB
RLB
LAB
LULB
LLB

No Biopsy Biopsy of:

PRE-ZERO HISTOLOGY

DATE	SITE	READING	SP NO. (& NOS)

LABORATORY DATA:

CYTOLOGY

Results Type of Preparation

HCT _____ Not Done
MBC _____ HGB _____ Sputum
% MBC _____
OTHER RESP. FUNCTION TESTS: Broncho.
PI. Fluid
AFB: Other

OTHER PARACLINICAL DATA:

GROSS PL. FLUID:

Reported Ave. Wt. _____ Calcul. Ave. Wt. _____
Adm. Wt. _____ Calcul. Wt. Loss _____
Reported Wt. Loss _____ Percent Wt. Loss _____ %

ASSOCIATED EVENTS

4. THERAPEUTIC DATA

ZERO TIME:

PRECEDING ACTIVITIES

FIRST COURSE OF ANTINEOPLASTIC RX

LUNG SURGERY

Date: C P UNK
Pre-op Intent Rx Course No.

SURGICAL FINDINGS:

At Entrance:

Site of Apparent 1°:

In Mediastinum:

SURGICAL PROCEDURES:

Frozen Section:

Biopsy Site: C P UNK
Intra-op Intent

Excision: R LUNG RUL RAL RLL L LUNG LUL LLL

Reason No

Resection:

Intra-op Complic:

Prognostic Comments:

PATHOLOGY

REPORT: Cell Type: SP No.

Sites: Nodes:

Other:

METASTATIC SURGERY (During First Rx Course)

Procedure:

Date:

Surgical Findings:

Cell Type: SP No.

RADIOTHERAPY (During First Rx Course)

Site	Onset	Ended	Tumor Dose	Medium

CYTOTOXIC RX (During First Rx Course)

Drug: Onset:

Dose: Ended:

(Pt. Number)

Cancer of the Lung Card No. 2: GENERAL SUMMATION

YEAR OF ZERO TIME <input type="text"/> <input type="text"/> (1) (2)		AGE <input type="text"/> <input type="text"/> (3) (4)		SEX <input type="text"/> (5)	HOSPITAL STATUS <input type="text"/> (6)	CUSTOMARY CIGARETTES <input type="text"/> (7)	OTHER TOBACCO HABITS Pipes 1 Cigars 2 Snuff or Chewed 4 <input type="text"/> (8)
COMPLAINANT STATUS <input type="text"/> (9)	EXTRANEOUS LATROTROPIC STIMULUS <input type="text"/> (10)	PULMONARY CO-MORBIDITY Chronic Cough 1 Chronic Dyspnea 2 <input type="text"/> Chronic Pulm. Disease 4 <input type="text"/> (11)		PARIETAL SX AND TBC Pleuritic Chest Pain 1 Non-Pleuritic Chest Pain 2 <input type="text"/> Active TBC 4 <input type="text"/> (for 8 and 9 see Criteria) (12)			
BRONCHIAL SX Recent Cough 1 Rust, Blood Streaks, or Hemoptysis 2 <input type="text"/> Subjective Wheeze 4 (13)		PARENCHYMAL SX Recent Dyspnea 1 Single Infection 2 <input type="text"/> Recurrent Infection 4 (14)		FEATURES OF INFECTION Chills, Fever or Sweats 1 Pneumonia (Clinical Dx) 2 <input type="text"/> Cold or Flu 4 (15)		OTHER EVENTS Unresolved Pneumonia 1 Transient Primary Sx 2 <input type="text"/> Paraneoplastic Syndrome 4 (16)	
GENERAL SX Anorexia 1 Wt. Loss (as Complaint) 2 <input type="text"/> Weakness, Fatigue, or Significant Malaise 4 (17)		HPO Clubbing Noted by Pt. 1 Significant Clubbing Noted by M.D. 2 <input type="text"/> Joint Pain Due to HPO 4 (18)		MEDIASTINAL SX Dysphagia 1 Hoarseness (NMVC or NEVC) 2 <input type="text"/> SVC Syndrome 4 (19)			
REGIONAL METASTATIC SX Horner's Syndrome 1 Brachial or Peripheral Arm Nerve SSx 2 <input type="text"/> Sx in Outer Thoracic Structures 4 (20)		DISTANT METASTATIC SX Non-Thoracic Bone Pain 1 Peripheral Neurologic SSx or Other 2 <input type="text"/> Cerebral Neurologic SSx 4 (21)		PROBLEMS IN ATTRIBUTION Primary Sx of ?-Attrib. 1 Systemic Sx of ?-Attrib. 2 Metastatic Sx of ?-Attrib. 4 <input type="text"/> (22)		CLINICAL GROUP <input type="text"/> (23)	
EVIDENCE OF WEIGHT LOSS <input type="text"/> (24)	ANCILLARY DATA Anemia 1 Elevated VP 2 Hypercalcemia or Other 4 <input type="text"/> (25)		SPUTUM CYTOLOGY; MEDIASTINOSCOPY <input type="text"/> (26)		GROSS PLEURAL FLUID <input type="text"/> (27)		
RESPIRATORY RESERVE Test Abnormal 1 M.D. Statement re Poor Ventilation 2 <input type="text"/> Severe Dyspnea 4 (28)		BRONCHOSCOPY FINDINGS <input type="text"/> (29)	BRONCHOPATHOLOGY OR LUNG BIOPSY <input type="text"/> (30)		CLINICAL ANATOMIC EVIDENCE Palpable Thoracic Metastasis 1 Palpable Surface Metastasis 2 Liver or Other 4 <input type="text"/> (31)		

EXTRAPULMONIC MORPHOLOGIC EVIDENCE				PRE-TREATMENT MICROSCOPY		RADIOGRAPHIC DESCRIPTION	RADIOGRAPHIC LOCALIZATION	
Regional Node	1	Pericardial Involvement	1				Primary Site	Vertical Location
Pleura, Pleural Fluid, Chest Wall or Thoracic Bone	2	Contralateral Site	2					
Contiguous Involvement	4	Ultrathoracic Site	4	(34)	(35)	(36)	(37)	(38)

RADIOGRAPHIC INVOLVEMENT							
MEDIASTINAL		IPSILATERAL THORACIC		CONTRALATERAL THORACIC		ULTRATHORACIC	
Definite Hilar Nodes	1	Pancoast Tumor or Pleural Effusion	1	Questionable Involvement or Pleural Effusion	1	Extrathoracic Bone	1
Definite Mediastinal Nodes	2	Peripheral Primary or Contiguous Involvement	2	Hilum or Mediastinum	2	Liver or Other	2
Mediastinal "Viscera"	4	Isothoracic Structures	4	Other Contralateral Structures	4	CNS	4
	(39)		(40)		(41)		(42)

ANATOMIC GROUP		ADDITIONAL PROGNOSTIC CO-MORBIDITY		ONCOGENIC		CONTRA-THERAPY REASONS		NON-ONCOGENIC	
		Severity of Tumor Effects	1	Juxta-Carinal or Cell Type	1	Low Respiratory Reserve	1		
		Signif. Cardiovascular Disease	2	Metastasis of Tumor	2	Co-Morbid Disease	2		
		Other Co-Morbid Conditions	4	Functional Severity of Tumor Effects	4	Other	4		
			(44)		(45)		(46)		

FIRST THERAPEUTIC ACTION	OTHER THERAPEUTIC CONSIDERATIONS	SURGICAL PROCEDURE AND INTENT	FURTHER SURGICAL DESCRIPTION	SURGICAL HISTOLOGY	SURGICAL PATHOLOGY
			Other Structures Excised, or Involved but 1" not Excised		
			Post-op. Complications		
			Op. or Post-op. Death		
				(51) (52)	(53)

SUBSEQUENT TREATMENT		ATTRIBUTION CERTAIN		ATTRIBUTION UNCERTAIN	
Surgery to Primary Site	1	New Endopulmonic or Systemic Manifestations of Tumor	1	New Endopulmonic or Systemic Manifestations of Tumor	1
Radiation to Primary Site	2	New Evid. of Thoracic Involvement	2	New Evid. of Thoracic Involvement	2
Systemic or Metastatic Treatment	4	New Evid. of Ultrathoracic Involvement	4	New Evid. of Ultrathoracic Involvement	4
	(54)		(55)		(56)

SUBSEQUENT NEW MORPHOLOGIC EVIDENCE	SUBSEQUENT MICROSCOPIC EVIDENCE	MODE OF DEATH	ASSOCIATED DISEASES
Isothoracic		Circumstances Unknown	Coexistent Other Cancer
Contrathoracic		Sudden or Unexpected	Coexistent Tuberculosis
Ultrathoracic		Definitely or Probably not Due to CA Lung	Necropsy Detection

NECROPSY FINDINGS	NECROPSY TISSUE	PRE-TREATMENT INTERVAL (' to ZT)	POST-TREATMENT INTERVAL (ZT to End)

SPECIAL COMMENTS	CARD NUMBER	ADDITIONAL DATA	PATIENT NUMBER
Special Note	0 2	Reversible Co-Morbid Wt. Loss	
Histology Discrepancy	(74) (75)	Additional Card	
Histology Disparity		Pre-Zero Morph. Evid. of Brain Involvement	

Cancer of the Lung

Card Number 3 : General Summation

Pt. Number

Race

T Evidence

TNM Stage

☐
(1)

T_3 T_2 T_1
☐ ☐ ☐ ☐
(2) (3) (4) (5)

T N M **Stage**
☐ ☐ ☐ ☐
(6) (7) (8) (9)

New Techniques in Imaging :

Study

Result

Associated Clinical Evidence

Liver/Spleen Scan

☐
(10)

☐
(11)

Brain Scan

☐
(12)

☐
(13)

Bone Scan

☐
(14)

☐
(15)

Acta Scan

☐
(16)

☐
(17)

Ultrasound

☐
(18)

☐
(19)

Gallium Scan

☐
(20)

☐
(21)

Other

☐
(22)

☐
(23)

**Toponymic Stage
Without Results From
New Techniques**

☐
(24)

**Toponymic Stage With
Equivocal Results From
New Techniques**

☐
(25)

**TNM Stage
Without Results From
New Techniques**

T N M **Stage**
☐ ☐ ☐ ☐
(26) (27) (28) (29)

**TNM Stage With
Equivocal Results From
New Techniques**

T N M **Stage**
☐ ☐ ☐ ☐
(30) (31) (32) (33)

Functional Severity

☐
(34)

Toponymic Stage

☐
(35)

Composite Stage

☐
(36)

Card Number

☐ ☐
(75) (76)

Patient ID Number

☐ ☐ ☐ ☐
(77) (78) (79) (80)

CRITERIA FOR CODING

Cancer of the Lung

Card No. 2: GENERAL SUMMATION

This revision was completed in March, 1972. It supplants the previous criteria, used for coding the analogous format marked Card No. 1: GENERAL SUMMATION.

These criteria were compiled by Dr. Feinstein and his Clinimetric research group.

(1), (2): YEAR OF ZERO TIME

The criteria for determining zero time, the inception event ("*" event), and zero state in a patient's clinical course are stated in Appendix A. The year of zero time is directly coded as '53, '54, ..., '59, '60, ..., etc. in columns 1 and 2.

(3), (4): AGE

Code in years as of last birthday before zero time.

(5): SEX

- 1: Male
- 2: Female
- 3: Male; stopped cigarette smoking, definitely before inception event
- 4: Female; stopped cigarette smoking, definitely before inception event
- 5: Male; decreased cigarette smoking, definitely before inception event,
but patient continued smoking
- 6: Female; as in 5

(6): HOSPITAL STATUS

Code the status and the hospital at which zero time occurred. An exception to this rule is the situation in which the diagnostic work-up and therapeutic decision occurred during an admission to one of our index hospitals, but the chosen zero-time treatment was administered elsewhere. In this circumstance, the patient's status at our index hospital is acceptable for the coding here. (The numbers and letters in parentheses refer to the coding citations used by the Admission Office at Yale-New Haven Hospital.)

- 1: Yale Private (1A, 1B, 1C, 1D, or 1E)
- 2: Yale Semiprivate (SP-2, P-2, SP-3, P-3, SP-4, or P-4)
- 3: Yale Ward (SP-6, S-6, SP-5, S-5, or SP-4-T)
- 4: Other [non-VA] hospital
- 5: West Haven VAH
- 6: Other VA hospital or Federal hospital (e.g., U.S.P.H.S. hospital)
- 7: Yale Out-Patient Department
- 8: Office of private doctor
- 9: Referred only for necropsy

(7): CUSTOMARY CIGARETTES

Code the amount (in packs per day) that represents the patient's most common mode of cigarette smoking before the "*" event.

- 0: None
- 1: Rare or < 1/2
- 2: 1/2
- 3: 1/2 to 1
- 4: 1
- 5: 1 to 2
- 6: 2
- 7: >2
- 8: Smoked, but amount UNK (used for descriptive terms such as "heavy",
"chain", "moderate", or "light" smoker)
- 9: UNK re cigarette smoking

- 2 -

(8): OTHER TOBACCO HABITS

Code as cited if patient ever engaged in these habits, even if he has stopped.
Code as 0 if UNK.

(9) - (10): IATROTROPY

The coding of columns 9 and 10 depends on the types of symptoms in the "present illness", on the iatrotropic stimulus, and on the diagnostropic stimulus.

The iatrotropic stimulus (I.S.) is the event or chain of events that evoked the clinical work-up that led to the occurrence of zero time. The diagnostropic stimulus (D.S.) is the event or manifestation(s) that made the doctor(s) decide to look for evidence of lung cancer. Going backwards from zero time, we first ask the question, "What event provoked the doctor(s) to search for evidence of lung cancer in this patient?". The answer to this question is the diagnostropic stimulus. We then ask the question, "What event provoked the patient to consult the doctor(s) who did the work-up (or who referred the patient for the work-up) that contained that diagnostic search?". The answer to this question is the iatrotropic stimulus.

The iatrotropic stimulus is often, but not always, the same as the "chief complaint" (C.C.) of the "present illness" that preceded zero time. The I.S. will usually differ from the C.C. in patients who are asymptomatic (so that there may be no C.C.), in patients whose C.C. has had a long duration, or in patients with a plethora of complaints. The diagnostropic stimulus is usually the same as the iatrotropic stimulus, but may differ in circumstances in which the initial complaints do not suggest lung cancer, or in which the diagnostically provocative events occur in a patient who has been chronically hospitalized for a temporally distant iatrotropic stimulus. If the D.S. occurs as the direct result of the work-up begun in response to the original I.S., that original event is regarded as the I.S. If the D.S. occurs as the result of new events that began after the work-up for the original I.S. was completed without a diagnosis of lung cancer, then the new D.S. is regarded as the I.S. for that patient.

These principles are illustrated in the cases that follow:

(a) The initial I.S. is the fever, cough and chest pain of a pneumonia that is at first not suspected as related to neoplasia. When the patient's X-ray fails to improve, the "unresolved pneumonia" then leads to a work-up for lung cancer. In this situation, the unresolved pneumonia is the D.S., having been provoked by events noted during the infectious episode. For such "intra-episodic" discoveries, the original clinical symptoms of the infection are coded as the I.S.

(b) Psychotic behavior is the I.S. for a patient who then receives long-term hospitalization for a "chronic brain syndrome". After five years in the hospital, this patient develops hemoptysis as the D.S. that leads to the identification of lung cancer. In this situation, the D.S. would be coded as the I.S.

(c) After completion of a clinical episode diagnosed and treated as infectious pneumonia (i.e., viral, tuberculous, or other bacterial), the patient is left with a pulmonary shadow that is re-examined periodically with X-ray. On one of the periodic X-rays, the shadow is found to be larger, and a work-up is instituted that leads to a diagnosis of lung cancer. In this case, the routinely

- 3 -

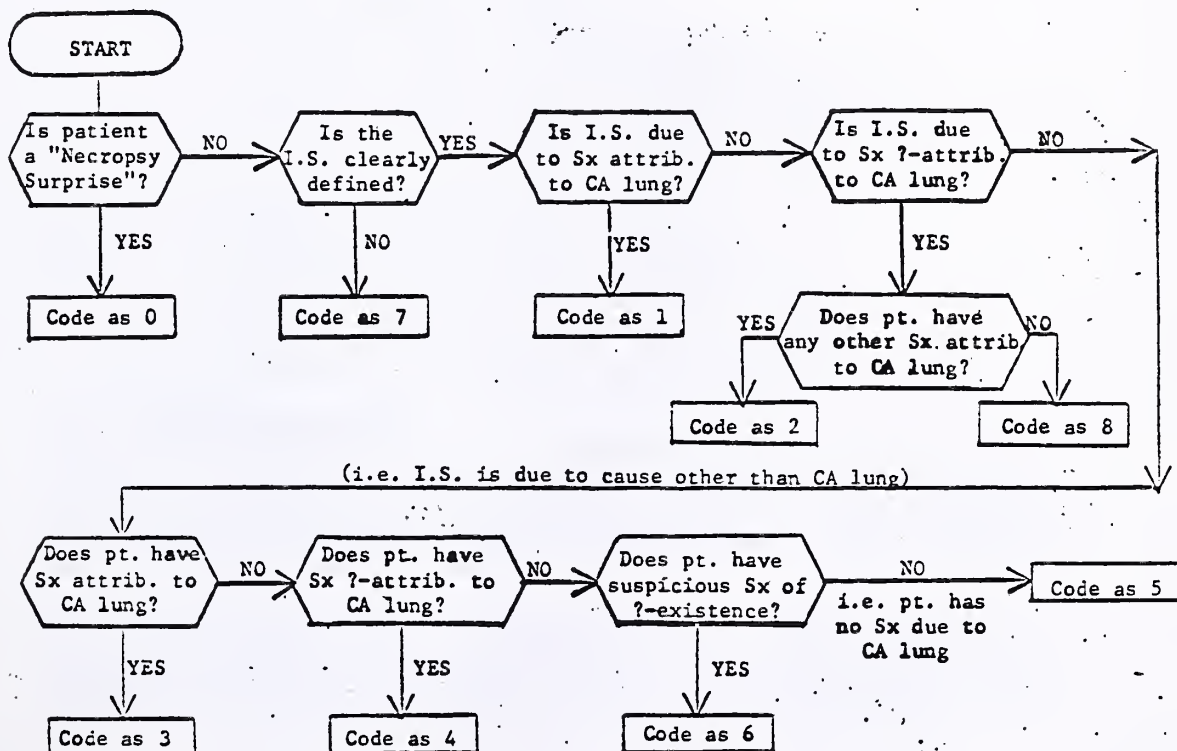
scheduled X-ray examination is the D.S., having occurred as a "post-episodic" event, at some time after completion of the original clinical episode and after the persistent shadow had not acted as a D.S. In such temporally remote "post-episodic" discoveries, the D.S. is coded as the I.S.

(d) A patient with psychotic behavior is committed to a state hospital and shortly afterward is transferred to another hospital for long-term care. At the second hospital, a routine admission X-ray film shows the pulmonary lesion for which the patient is then referred to an index hospital where he receives the diagnostic work-up that shows lung cancer. The psychotic behavior is the I.S., and the admission X-ray at the second hospital is the D.S. Since this D.S. was a routine procedure, presumably performed on all patients regardless of their clinical state, the psychotic behavior is coded as the I.S.

(9): COMPLAINANT STATUS

This coding depends on many variations in the data available in a patient's medical record. The identity of the I.S. may or may not be clearly determined, and its attribution may be certain or uncertain. "Suspicious" symptoms (i.e., those that can be attributed or ?-attributed to lung cancer) may also be present, questionably present, or absent.

The following flow chart shows how these different variations are managed for choosing the coding numbers for the I.S. in this column:



- 4 -

With these conventions, the coding for column 9 can be simply listed as follows:

- 0: Not applicable, "necropsy surprise"
- 1: I.S. due to Sx attrib. to CA lung
- 2: I.S. of uncertain attribution. Pt. has other Sx attrib. or ?-attrib. to CA lung
- 3: I.S. due to cause other than CA lung. Pt. has Sx attrib. to CA lung
- 4: I.S. due to cause other than CA lung. Pt. has Sx ?-attrib. to CA lung
- 5: No "Sx suspicious" of CA lung
- 6: I.S. due to cause other than CA lung. Pt. has suspicious Sx of ?-existence
- 7: I.S. not clearly determined or identified
- 8: I.S. of uncertain attribution. Pt. has no other Sx attrib. to CA lung

For patients who are "necropsy identification" cases -- i.e., tumor suspected in life, but primary source not identified until necropsy -- this column should be coded with the I.S. selected on basis of the examinations that led to the diagnosis and/or treatment of cancer.

For patients whose I.S. is due to "cause other than CA lung" (i.e., patients coded with 3, 4, 5, or 6), a positive response must be entered in column 10.

(10): EXTRANEOUS IATROTROPIC STIMULUS

- 0: Not applicable [0, 1, 2, 7, or 8 in column 9]
- 1: Sx of other disease; probably not related to CA lung
e.g. Hernia (without cough); hemorrhoidal bleeding; urinary retention
- 2: Sx of other disease; relation to CA lung unclear
e.g. Newly developed diabetes mellitus; Sx of peptic ulcer
- 3: Sx of other disease; probably related to CA lung
e.g. Hernia (with cough)
- 4: Regular follow-up of a chest disease
e.g. TBC; chronic lung disease; previous shadow
- 5: "Routine" test: not further specified
e.g. "Mobile unit"; "routine check-up"
- 6: "Routine" test imposed on patient or pre-scheduled
e.g. Factory survey; employment film; annual exam; veteran's benefits; son's TBC skin test positive in school

(11): PULMONARY CO-MORBIDITY

The cited entities are coded here regardless of their prognostic or contra-therapeutic significance. Cough or dyspnea should be persistent to be coded; do not code these entities if they disappeared well before zero time, or if they occurred only in isolated past episodes. The only pulmonary co-morbid conditions not cited here are "Active TBC", which is coded in column 12, and low "Respiratory Reserve", which is coded in column 28.

Only chronic entities may be coded in this column; recent cough and dyspnea are coded in columns 13 and 14. A manifestation such as cough or dyspnea is clearly chronic if the patient says it has been present for an unquantified but definitely long period of time, such as "all my life" or "for many years". On the other hand, the cough or dyspnea is clearly recent if the patient assigns to it a

- 5 -

specific duration that is shorter than the duration of time from the inception event.

For the cases in which the cough or dyspnea may itself be a candidate for inception event, we have adopted the following convention for consistency in classification. Cough or dyspnea that has persisted for 10 years or less without an apparent cause other than lung cancer is considered recent and may therefore be assigned to the "*". The symptom is then coded appropriately in column 13 or 14; if the duration is more than 10 years, the entity is considered chronic and is coded in column 11.

Chronic Cough: A past diagnosis of "chronic bronchitis" should not be coded here unless a cough is specifically mentioned. See previous comments for definition of "chronic".

Chronic Dyspnea: In elderly patients, "2-flight dyspnea" is not designated as dyspnea unless accompanied by a statement that the exertion was interrupted by the need to rest. "Three-flight dyspnea" is ignored unless specified as a significant worsening in respiratory capacity. "Two-pillow orthopnea" is not regarded as orthopnea unless there is reasonable evidence or presumption that the pillows are used to elevate the upper torso, rather than the head alone. An M.D. statement of low respiratory reserve is coded in column 28, not here.

Chronic Pulm. Disease: This entity is coded when a definite co-pulmonary disease is diagnosed clinically. An X-ray diagnosis alone does not suffice. This category includes such citations on the extraction form as "significant emphysema", "CPD", "silicosis", and "pulmonary fibrosis". Do not code "asthma" or "bronchitis" unless they are medically documented.

(12) - (15): PRIMARY SYMPTOMS

The primary symptoms coded in columns 12-15 need not be present at zero time and can be coded as long as they have had a distinct existence during the "present illness". The TBC entry in column 12 is not a primary symptom, and is included here only for convenience in the coding format.

(12): PARIETAL SX AND TBC

The term "parietal symptoms" refers to chest pain that is definitely or possibly attributable to the lung cancer or to surrounding inflammation. Excluded from this coding are a thoracic pain that lasts no more than several hours or a pain that occurs uniquely with exertion and subsides with rest.

The object here is to describe the totality of "suspicious" chest pain regardless of whether the totality included one, two or more different types and locations of pain. Note that the 1, 2 and 4 parts of this coding are used additively. Thus, pleuritic and non-pleuritic pain in a single location would be a 3 and two different pains (one pleuritic and one non-pleuritic) in two separate locations would also be 3. When the pleural characteristic of one chest pain is known but the pleural aspect of a second pain is unknown, code only the known pain. Use the 8 or 9 codes (as described later) only when the pleuritic aspect of all existing chest pain is unknown. Note that a chest pain can be coded here and also in column 20 when appropriate.

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When TBC is coded here, category 2 of column 61 should also be coded unless subsequent evidence was obtained to demonstrate that the pre-zero diagnosis of TBC was fallacious. The refutational evidence can come from surgery or necropsy. If the evidence of TBC occurred only after zero time, or before the "present illness", code the 2 in column 61 and do not code here. Thus, if 4 is coded here and 2 is not coded in column 61, the implication is that the pre-zero diagnosis of TBC was erroneous. If TBC is coded here and in column 61, we are left unsure of whether it occurred before or during the "present illness".

1: Pleuritic Chest Pain: A pleuritic pain is one that is noted as pleuritic" or "inspiratory" (increased with deep breathing, inspiration, yawning or straining). A pain that occurred or increased only with coughing is not coded as pleuritic if the pain appeared to be due only to tracheal irritation (i.e., midline location).

2: Non-Pleuritic Chest Pain: A non-pleuritic pain is one that was cited as "non-pleuritic", or that is specifically stated to have none of the characteristics just noted for "pleuritic" pain.

4: Active TBC: Code this category if tubercle bacilli were demonstrated and/or if the patient received deliberately chosen anti-tuberculous treatment during the interval between the inception symptom and zero time. "Demonstration" of tubercle bacilli includes a positive smear or culture, or intra-animal growth. Anti-tuberculous therapy includes treatment with INH, PAS, streptomycin or other preparations specified as anti-tuberculous; or treatment in a TBC sanatorium with bed rest or other "nutritive" or salubrious procedures.

8: Type of Chest Pain Unknown: Code when the pleuritic aspect of all chest pain is unknown, and there is no evidence of "Active TBC".

9: Active TBC and Type of Chest Pain Unknown: Code when the pleuritic aspect of all chest pain is unknown and the patient has evidence of "Active TBC".

(13): BRONCHIAL SX

Recent Cough: See the earlier comments about "chronic" and "recent" in column 11. The term "recent" can refer to an entirely new cough, or to a change in pattern of a chronic cough.

Rust, Blood Streaks, or Hemoptysis: This category can be used for any of the various ways in which a patient can cough blood, such as liquid blood, clots, flecks, streaks, or "rusty" sputum.

Subjective Wheeze: The wheeze should be recent, and subjectively noted and reported by the patient, regardless of whether or not a wheeze is noted on physical examination.

(14): PARENCHYMAL SX

Recent Dyspnea: Before coding, verify that the symptom is both

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"recent" and "dyspnea" as cited earlier in column 11. In a patient with pleuritic chest pain, beware that "dyspnea" has not been reported erroneously as a description for shallow breathing or "short-windedness", and look for an exertional or positional distinction that can help clarify the situation.

Single Infection: A "single infection" is one that qualifies as an infection, as cited in column 15, and that occurred as a continuous episode of illness -- even though the manifestations may have fluctuated during that episode. The episode is regarded as ended when the patient has entirely recovered, i.e., out of hospital, or back to the usual state that existed before the episode; after this time, new infectious manifestations would be regarded as a "recurrent infection". A reappearance of infectious symptoms while therapy is being discontinued or during the convalescent period is not regarded as a new episode of infection.

Recurrent Infection: The patient should have had two or more distinct episodes of an illness qualified in column 15 as an infection. The episodes should have been separated by a time interval during which the patient was not receiving anti-infectious treatment and was in his usual state of previous health. If no distinct decision can be made between "single" or "recurrent", code the infectious events as "single".

Note: If 2 or 4 is coded in column 14, a "feature of infection" must be coded in column 15.

(15): FEATURES OF INFECTION

The object here is to indicate pulmonary infections, not non-specific inflammations of the upper respiratory tract. These two topographic entities may easily be confused, because after a patient is discovered to have an abnormal shadow on chest X-ray, retrospective history-taking may evoke a story of infectious symptoms that were not particularly prominent or diagnostic, and that may have been due to upper rather than lower respiratory ailments. The symptoms most likely to be truly in the lower respiratory tract are those that evoked the chest X-ray, rather than those whose existence was first described after the X-ray was noted to contain a lesion.

Chills, Fever of Sweats: No inherent characteristics of these entities can distinguish their source as a lower or upper respiratory infection. These symptoms are likely to be associated with a lower infection, however, if accompanied by hemoptysis or significant physical findings in the chest, or if they evoked a chest X-ray. Fever occurring after the patient was admitted to the hospital should be coded here only if cogent. A "cogent" fever is persistent (i.e., more than a single isolated reading), high (i.e., more than a minor "spike" above normal range), and has sufficient impact on the doctor to evoke specific diagnostic or therapeutic measures for it.

Pneumonia (Clinical Dx): This entity is coded in at least two kinds of situation:

(a) A hospitalized patient has been treated with antibiotics for a pulmonary shadow, or the diagnosis of pneumonia has been stated in a progress note or on the diagnostic sheet. This definition of "pneumonia"

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does not pertain to a roentgenographic shadow and/or antibiotic therapy associated with unequivocal pulmonary tuberculosis.

(b) At some time in the past, but still within the time boundaries of the "present illness", a non-hospitalized patient was told he had "pneumonia".

Cold or Flu: This is the weakest type of evidence for denoting pulmonary infection, and this entry should be coded only in the following circumstances:

(a) In the absence of chills, fever, or sweats, the coryzal symptoms acted as a diagnostropic stimulus for the chest X-ray, although a diagnosis of cancer rather than pneumonia was made at X-ray. (If the X-ray diagnosis was "pneumonia", mark the preceding entry as well as this one).

(b) The patient's symptoms appear related to the lung cancer, but are described no more specifically than "cold" or "flu".

This entry should not be coded if the patient has only the following:

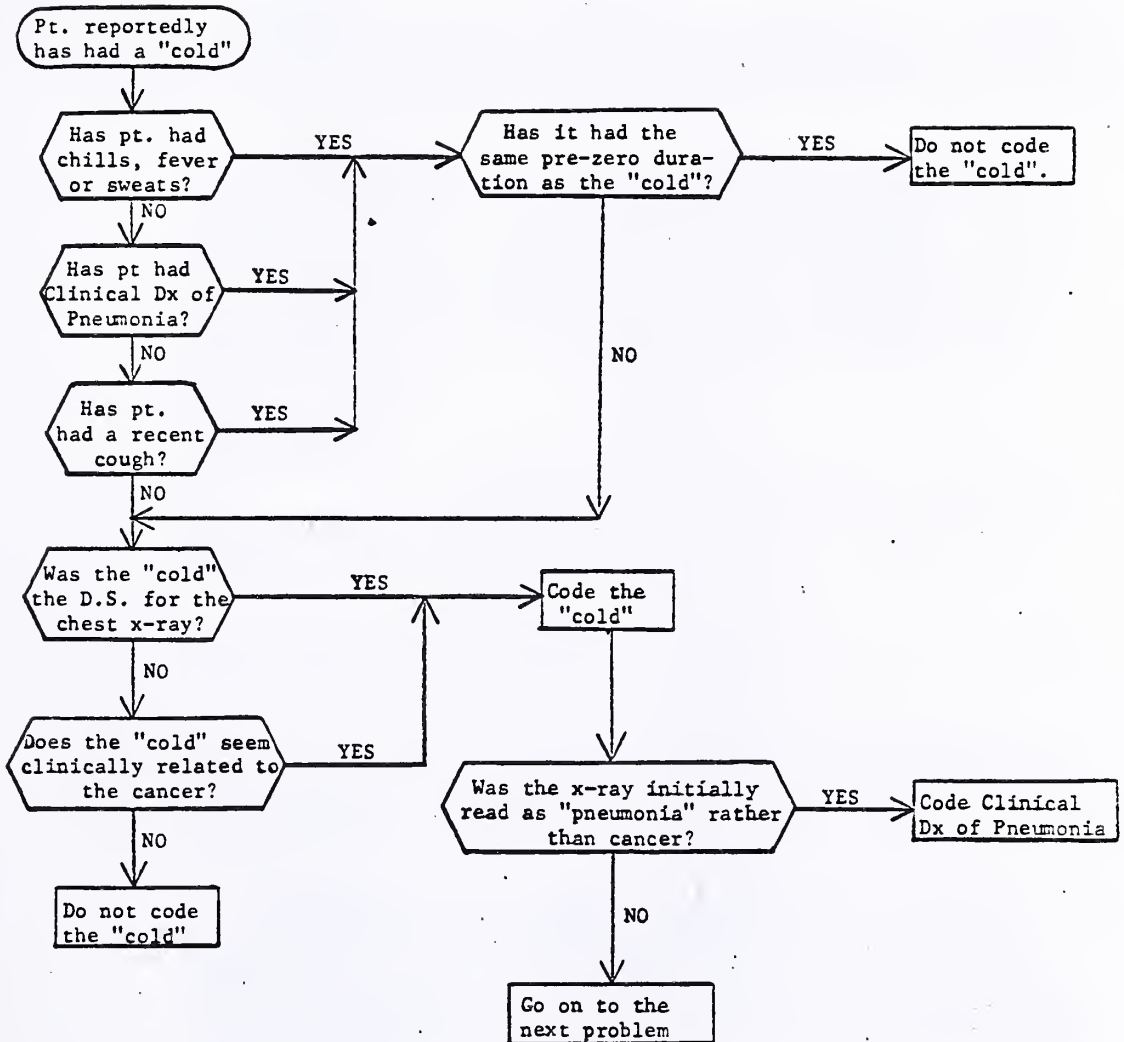
(a) A recent cough of the same duration as the "cold" or "flu", and no other cited "infectious symptoms".

(b) One of the cited "infectious symptoms", and/or a clinical diagnosis of pneumonia, that has the same duration as the "cold" or "flu".

An algorithm for coding this entity is shown as a "flow chart" on the next page.

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Flow Chart for Coding "Cold" or "Flu" in Column 15



Note: Throughout this flow chart, the term "cold" represents either "cold" or "flu".

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(16): OTHER EVENTS

The entities cited here are assembled in one column solely for convenience in the coding format. The category marked 1 (Unresolved Pneumonia) can be "added" to either the 2, 4, 6 or 8 category to create a 3, 5, 7 or 9 coding; but all other categories are mutually exclusive.

1: Unresolved Pneumonia: Code when a presumptively inflammatory lesion (TBC, pneumonia, etc.) fails to resolve on X-ray and the absence of radiographic resolution acts as the diagnostropic stimulus for the work-up for cancer of the lung. In this clinical situation, the patient is initially regarded as having an acute infectious pneumonia, which may be viral, bacterial, or tuberculous, and which is confirmed by X-ray. After a period of appropriate therapy for the pneumonia, the chest X-ray fails to clear, or the lesion may even enlarge. At this point, the physician begins to suspect lung cancer and orders a further work-up to confirm his suspicion.

The unresolved pneumonia coding should not be used for the following circumstances:

(a) The initial X-ray provided a diagnostropic stimulus. Such a situation is exemplified by a patient who was treated at home for symptoms of infection without roentgenography, and who later shows an abnormal shadow on X-ray.

(b) The diagnostropic stimulus was provided by a positive result in the initial sputum pap smear, ordered routinely at the time the patient was admitted with pneumonia.

(c) A change in a long-standing lung shadow, initially found in a routine screening examination or during an episode of pulmonary disease, is noted on routine follow-up examination. The change elicits a work-up for lung cancer. Because of the temporal remoteness from the original discovery of the shadow, its change is not regarded as "unresolved pneumonia", and will usually be coded in category 4 of column 10.

2: Transient Primary Sx: In some patients with primary symptoms only, all of the symptoms may have disappeared before zero time. Such a circumstance is particularly likely when the symptoms have consisted exclusively of hemoptytic, infectious, or pleuritic manifestations or various combinations of these. In such situations, the disappearance of all previous symptoms, rendering the patient essentially asymptomatic at zero time, can be cited here. "Transient Primary Symptoms" is intended to deal with such situations as:

(a) A patient with a single episode of cough and fever six weeks ago, and none since then; or

(b) A patient whose only symptom is recurrent episodes of hemoptysis that stopped well before zero time.

4: Paraneoplastic Syndrome: This category refers to a clinical "systemic" syndrome, other than HPO, attributed to products of the tumor.

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Such syndromes can include gynecomastia (when attributed to a "hormonal effect" of the lung tumor); carcinoid syndrome; inappropriate secretion of anti-diuretic hormone (vasopressin or ADH); and hypercalcemia. To be coded here, the syndrome must have produced distinct clinical symptoms or overt signs. If these clinical manifestations were not present, and the syndrome was identified by laboratory evidence alone, the laboratory findings should be coded in column 25. The latter situation is particularly likely to occur with hypercalcemia or the ADH abnormality. Note that "hormonal" neuropathy or neuromyopathy is not coded in this category.

6: "Metastatic" Paraneoplastic Syndrome: Certain neurologic manifestations are suggestive of a "hormonal" neuropathy or neuromyopathy. (E.G. Ataxia and gait disorder without hemiparesis or hemiplegia would imply a cerebellar disorder of uncertain source.) Although a specific anatomic metastasis usually cannot be ruled out, such neurologic manifestations may be coded here when a "hormonal" cause is suspected. (Do not also code the neurologic entity separately in column 21.) Although "distant" sites can be affected in a paraneoplastic syndrome, the "systemic" (rather than "metastatic") character of the manifestations is usually denoted by paraclinical evidence (e.g., Cushing's syndrome) and or by the absence of X-ray or other anatomic evidence of metastasis (e.g., hypercalcemia without bone lesions). Such "systemic" manifestations are coded in category 4, not here.

8: Systemic and "Metastatic" Paraneoplastic Syndrome Code this category if the patient qualifies for both the 4 and 6 categories of coding.

(17) - (18): SYSTEMIC SYMPTOMS

In addition to the entities cited in columns 17 and 18, this class of symptoms includes the paraneoplastic clinical syndromes cited in category 4, 6, or 8 of column 16.

(17): GENERAL SX

Anorexia: This symptom should have been persistent and not just a brief period of loss of appetite associated with infectious symptoms.

Wt. Loss (as Complaint): To be coded here, weight loss must be a chief complaint, or one of the main complaints. It should not have been merely a "symptom" noted during routine questioning about the Present Illness or Review of Systems.

Weight loss, particularly when regarded only as a symptom, cannot ordinarily have its cited duration used as a significant chronometric entity for determining such items as timing of the inception event or iatrotropic stimulus. For weight loss to have chronometric "dignity" there must exist evidence to substantiate the duration during which the weight loss occurred. Such evidence can consist of one or both of the following: (a) regular weight examinations at frequent intervals, showing a declining value of weight; (b) an observed change in fit of an appropriate piece of clothing (e.g., belt, trousers, dress) whose fit was frequently

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assessed during the alleged period of weight loss. These requirements would pertain only when the weight loss is said to have occurred over a long period of time, such as more than six months. A span of less than six months requires individual decisions. If weight loss is a chief complaint, its chronometric validity is more acceptable than if it is merely a symptom.

Weakness, Fatigue, or Significant Malaise: "Weakness" here refers to general muscular weakness. It does not refer to any localized weakness in a single extremity or to the weakness associated with focal involvement of the spinal cord or nerve roots. To be cited here, any one of these three symptoms should have been persistent, and not just a transient event associated with infectious symptoms.

(18): HPO [Hypertrophic Pulmonary Osteoarthropathy; sometimes also called "Periostopathy"]

Clubbing Noted by Pt.: Coded here only when the patient reported it as a recent (datable) appropriate change in the shape of his fingertips or toes.

Significant Clubbing Noted by M.D.: In an effort to avoid coding the many minor variations of fingertips that are cited as clubbing by over-eager examiners, clubbing is coded here only when it is unanimously agreed upon by all examiners or if it has been cited as "4+", "significant", "marked", or "unequivocal".

Joint Pain Due to HPO: The object here is to restrict the citation to an HPO type of joint pain, and to avoid coding joint pains due to various arthritides or to neoplastic metastases in bone. Consequently, the requirements for coding are: (a) pain in the articular segment of a long bone, (b) absence of some other form of joint disease at that site, and (c) no X-ray evidence of tumor at the affected site. Note that specific X-ray evidence of HPO is not required if the other three requirements are fulfilled. If X-ray evidence of HPO is present, requirement (b) can be ignored, but X-ray evidence alone is not satisfactory for coding in this column, i.e., appropriate pain must be present. If X-ray evidence of HPO exists without clinical signs or symptoms, code this evidence in column 25.

(19) - (21): METASTATIC SYMPTOMS

To be coded in columns 19 through 21, metastatic symptoms must be definitely attributable to the cancer. The eligible regions are described in greater detail in Appendix B.

(19): MEDIASTINAL SX

Dysphagia: This entity refers to difficulty after the act of swallowing is initiated. The symptom may also be expressed as "food getting stuck", "trouble in swallowing", etc. The coding citation requires that the dysphagia be a prominent and persistent symptom, but a positive barium esophagram is not required.

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Hoarseness (NMVC or NEVC): NMVC refers to "non-moving vocal cord"; but a report of "incomplete movement" is acceptable for this designation. NEVC refers to "non-examined vocal cord". Do not code this entity if the cord is examined and moves; in such a situation, the patient should have some other explanation for his "hoarseness", but if none is present, check for individual decisions about the coding. Do not code this entity if the cord is reported as non-moving but the patient is not reported to have "hoarseness" or some other difficulty in phonation.

SVC Syndrome: Refers to swellings of the upper torso (neck and/or arms) designated as the "Superior Vena Cava Syndrome". In the absence of such swelling, unequivocal or massive distention of visible veins on the upper thorax is acceptable evidence. In the absence of the cited evidence, an elevated venous pressure alone is not acceptable for this coding, and is indicated in column 25.

(20): REGIONAL METASTATIC SX

Horner's Syndrome: This coding requires the diagnostic statement of "Horner's Syndrome" or such acceptable constituents as unilateral ptosis, enophthalmos, miosis, or loss of sweating on the affected side of the face.

Brachial or Peripheral Arm Nerve SSx: These are manifested in such symptoms or observable signs as pain, numbness, tingling, or paresthesias in the arm or fingers, or difficulty in moving muscles of the arm or fingers. This coding requires simultaneous evidence of tumor in the apex of the lung or mediastinum of the affected side.

Sx in Outer Thoracic Structures: The eligible topographic regions are endothoracic bones (ribs, sternum, thoracic vertebrae), parathoracic bones (clavicle and scapula), parathoracic nodes, and chest wall constituents (muscles, thoracic nerves, subcutaneous tissue, and skin). For a more complete discussion of topography, see Appendix B. To be coded here, an involved bone must be painful, and must have either X-ray substantiation of involvement or a clinical decision to treat it with focal anti-neoplastic therapy. X-ray evidence is not required if pain is attributed to a non-bony structure in the chest wall. If appropriate, a symptom coded here may also be coded in column 12.

If the patient has reported a palpable thoracic mass, this "symptom" is coded here unless it is a non-contiguous subcutaneous mass, in which case it is coded as 2 in column 21. A "symptomatic" parathoracic node is always coded here, regardless of its contiguity. A thoracic mass noted on physical examination is coded appropriately in column 31, regardless of whether or not it was coded as a symptom in columns 20-21. When symptoms of the spine or spinal vertebrae are not specifically cited as ultrathoracic (i.e., cervical, lumbar or sacral) they are assumed to be thoracic (dorsal) and are also coded here.

(21): DISTANT METASTATIC SX

Non-Thoracic Bone Pain: The acceptable topographic sites are any bones other than those described in column 20 as "endothoracic" or

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"parathoracic". In addition to pain, the required evidence is either X-ray demonstration of metastasis (with or without fracture) or a clinical decision to treat the affected site with focal anti-neoplastic therapy.

Peripheral Neurologic SSx or Other: The peripheral signs and symptoms should not be in the arm, whose manifestations are coded in column 20. The most common peripheral manifestations to be coded here will be in the lower extremities, and can be caused either by direct metastatic involvement of nerves, or by bony or other metastases pressing on nerve roots or spinal cord. If the peripheral manifestations are exclusively muscular, a "hormonal neuromyopathy" should be considered.

The "other" part of this category refers to various ultrathoracic manifestations that have been reported as symptoms by the patient, such as ultrathoracic cutaneous or subcutaneous nodules. Manifestations such as jaundice (when attributable to hepatic or peri-hepatic metastases), pigmentation (when attributable to Addison's disease, presumably caused by metastases to the adrenals), or esoteric types of metastatic phenomena, are coded here if they are symptomatic or noted as overt signs by the examining physician.

Cerebral Neurologic SSx: The manifestations of cerebral metastases should be distinguished from those due to peripheral causes or co-morbid cerebral disease. The manifestations that suggest a cerebral lesion (in contrast to peripheral causes of neurologic symptoms) are lateralization of symptoms to one side of the face, arm, or leg; the absence of pain or paresthesia at the affected site; and evidence of spasticity (e.g. hemiplegia) in an affected extremity. Manifestations regarded as "cerebellar", such as ataxia, are acceptable. Such non-lateralized neurologic manifestations as headache, convulsions, disorientation, and obtundity are acceptable as significant cerebral phenomena provided they are persistent, and do not occur as terminal events in a moribund patient, or in association with other conditions simultaneously producing high fever, shock, etc. The attribution of cerebral lesions to metastases, rather than other causes, depends on the available evidence and on the decisions made by the attending physicians.

(22): PROBLEMS IN ATTRIBUTION

This column can be used in two different ways in reference to symptoms of uncertain attribution: (a) to indicate situations in which such symptoms, having been coded in columns 12-18, then served as major determinants of the "staging" decision for the clinical group coded in column 23; and (b) to indicate certain "metastatic" symptoms, of uncertain attribution, that were not coded in columns 19-21.

If the assignment of clinical grouping depends solely upon the inclusion of primary or systemic symptoms of uncertain attribution, category 1 or 2 is coded here.

1: Primary Sx of ?-Attrib.: The inclusion of primary symptom(s) of uncertain attribution in columns 12-15 may affect the chronometry or toponymy of clinical staging. Problems arising from either of these

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circumstances are cited in this category. The coding of this category is illustrated by the following cases:

(a) Example of chronometric distinction: In a patient with chronic lung disease, the reported inception event is a change two years ago in his chronic cough. Three months before the admission during which zero time occurred, he noted the onset of hemoptysis which has been definitely attributed to the lung cancer. The patient has no "systemic" or "metastatic" symptoms. Both cough and hemoptysis are coded in column 13. The patient will be classified in Clinical Group 2, "Long Pulmonic", solely on the basis of the cough, which is only questionably attributed to cancer of the lung; but if the cough were not regarded as a neoplastic symptom, the Clinical Group would be 3, "Short Pulmonic". Code 1 in column 22 to indicate the chronometric influence of the cough.

Note: Without the inclusion of this symptom of questionable attribution, the patient's clinical stage would have been higher.

(b) Example of toponymic distinction: A patient admitted with hemoptysis, chills, fever, and cough is found to have active tuberculosis and lung cancer. The symptoms are all coded in columns 12-15, but none can be definitely attributed to his lung cancer. He has no "systemic" or "metastatic" symptoms, and his clinical group will be designated in column 23 as 2 or 3, according to the duration of the symptoms. Code 1 in column 22 to indicate that all of the "primary" symptoms are only questionably attributable to cancer. (The 1 would not be entered if any one of the "primary" symptoms were distinctly attributable to the cancer.)

Note: Without the inclusion of the symptom(s) of questionable attribution, the patient's Clinical Group would have been lower, since he would be asymptomatic with respect to his lung cancer.

Category 1 should not be coded if the patient has any "systemic" or "metastatic" symptoms that are definitely attributed to the cancer. The category should also not be used in the absence of a problem in primary-symptom attribution, merely to indicate that the coding of Clinical Group has been affected by chronometric uncertainty. An example of uncertainty in chronometry but not in symptom attribution is as follows:

(c) A patient is admitted with a history of fever, hemoptysis and chest pain for three months, according to two observers. One observer reports that the patient also has had a cough for three months, while the other states that the cough began one year ago. Since the patient has no co-pulmonary ailments, all of the primary symptoms are considered definitely due to his lung cancer, but according to the first observer, the coding for Clinical Group would be "Short Pulmonic" and according to the second, "Long Pulmonic". This chronometric ambiguity, arising solely from observer variability, is indicated only in columns 65-68

Systemic Sx of ?-Attrib.: Code here if all symptoms in columns 17, 18 and category 4 of column 16 are of uncertain attribution, and if no metastatic symptoms are coded in columns 19-21. For example, if a patient with active tuberculosis and lung cancer complained of cough, fever,

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hemoptysis, and generalized weakness -- all of questionable attribution -- and if he had no other symptoms, he would fall into the "systemic" category (4 in column 23) for clinical grouping. Code 2 in column 22 to indicate that his "systemic" grouping is based exclusively on a symptom of uncertain attribution. In addition, code 1 in this column, since the attribution of all his primary symptoms is also in question.

The 4 category in this column is coded when a "metastatic" symptom of the type cited in columns 19-21 was not coded in those columns because it had uncertain attribution.

Metastatic Sx of ?-Attrib.: If no other metastatic symptom has been coded in columns 19-21, an entry here will imply that a symptom of possible metastasis has been excluded from consideration for the clinical group coded in column 23. For example, in a patient who has no other metastatic manifestations, the symptom of "back pain" may not have been coded in column 21 because the X-ray was negative and the site was not considered for local anti-neoplastic therapy. A 4 is entered here to indicate that this back pain, although possibly due to metastasis, was not included among the symptoms used in coding column 23. If another metastatic symptom has been coded in columns 19-21, this category may be coded to indicate that a metastatic symptom of uncertain attribution has occurred in a region different from that of the entries coded in columns 19, 20, or 21. Thus, in a patient who has the type of back pain just described, and who also has the SVC syndrome, a 4 would be coded in column 19, a 4 in column 22, and a 5 in column 23. As another example, consider the development of jaundice in a patient with cirrhosis who is also paraplegic secondary to a lower vertebral metastasis demonstrable on X-ray. Because it is uncertain whether the jaundice is due to the patient's cirrhosis or to metastatic cancer, it is coded as a 4 in column 22, whereas the paraplegia is coded as a 2 in column 21.

(23): CLINICAL GROUP

The categories used here were developed arbitrarily for this research. They are based on the toponymic and chronometric spectrum of symptoms during the "present illness". The criteria for the categories listed below are found in Appendix C.

- 1: "Asymptomatic"
- 2: "Long Pulmonic"
- 3: "Short Pulmonic"
- 4: "Systemic"
- 5: "Metastatic"

(24): DOCUMENTED WEIGHT LOSS

Weight loss is not coded here if it is deliberate (i.e., part of a reducing program) or if it is attributable to a reversible co-morbid ailment (such as an active peptic ulcer, uncontrolled diabetes mellitus, an incarcerated hernia, etc.). Weight loss that appears to have "stabilized" for a substantial period of time is probably not due to the cancer and may have been associated with a reversible co-morbid ailment. Significant weight loss associated with a reversible, co-morbid ailment is coded as a 1 in column 76; minor weight loss associated with such an ailment is not coded at all.

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Significant weight loss (i.e., $\geq 10\%$ or ≥ 20 lbs. if % not calculatable) that is non-deliberate and "non-reversible" can be attributed definitely or probably to the cancer, definitely or probably to a co-morbid disease, or to uncertain attribution. Among the co-morbid diseases that can cause non-reversible weight loss are chronic debilitating conditions (severe rheumatoid arthritis, cardiac decompensation, poor pulmonary function) or another cancer (chronic leukemia). The co-morbid disease is particularly likely to be the cause of a non-reversible weight loss if the duration of the weight loss is quite long (years) or exceeds the duration of other symptoms attributable to the cancer. Conversely, in the presence of a chronic co-morbid disease whose condition has shown relatively little recent change, a recent weight loss is probably due to the cancer. If the weight loss is attributable to a "metastatic" manifestation (e.g. cerebral symptoms) that is itself of uncertain attribution, code the weight loss as though it were of co-morbid attribution.

In coding the categories of minor weight loss (7, and 8 below), distinctions of attribution are unnecessary and the appropriate amount can be coded directly. In coding the other categories, note that the term "cachexia" (or its congeners as listed below) takes precedence over any quantitative categories. If the cachexia is due to a non-reversible co-morbid disease, code 5.

Weight loss that is coded in categories 1-4 is eligible for usage in coding Iatrotomy (column 9) and Clinical Stage (column 23). Unless the timing of the weight loss is precisely documented (with repetitive weights, etc.), it is not eligible for coding in pre-zero chronometry (columns 65-68).

A complete documentation of weight loss requires three items of information: the patient's average ordinary weight, the reported amount of weight lost at zero time, and the weight at zero time. (The weight and weight loss noted at the admission during which zero time occurred can be used instead of the values at zero time). If two of the cited values are known but not the third, the coder may calculate the third, if the extractor has not done so already. If all three values are known, but do not add up correctly, an individual decision must be made about which value to reject. For example, a patient with an average weight of 170 lbs. may report a weight loss of 25 lbs., but may weigh 160 lbs. on admission. If the sequence of daily weights in the hospital seems consistent, the admission weight should be retained, and either the weight loss statement or the average weight statement should be rejected.

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The percentage of wt. loss = $100 \times (\text{amt. of wt. loss}) / (\text{average usual wt.})$.
The coding is:

- 0: No wt. loss, voluntary deliberate wt. loss, or wt. loss associated with "reversible" co-morbid disease

In categories 1-4, the weight loss is attributable or probably attributable to the lung cancer:

- 1: M.D. statement of "cachexia", "emaciated", or "inanition"
Code such a statement here, regardless of the quantity of weight loss
- 2: Wt. loss of $\geq 20\%$ in a relatively short period of time (usually 6 mos. or less)
- 3: Wt. loss of $\geq 20\%$ in a relatively long period of time (usually more than 6 mos.)
- 4: Wt. loss $10\% < 20\%$ or 20 lbs. or more [% not calculatable]

In categories 5-6, the weight loss is attributable or probably attributable to a non-reversible co-morbid ailment:

- 5: Super weight loss (i.e., cachexia or $\geq 20\%$)
- 6: Major weight loss (i.e., $10\% < 20\%$ or ≥ 20 lbs. if % not calculatable)

In categories 7-8, the weight loss is attributable to either the lung cancer, or to a non-reversible, co-morbid ailment:

- 7: Wt. loss $5\% < 10\%$ or 10-19 lbs. if % not calculatable
- 8: Some wt. loss but not as much as any of the above
- 9: Amt. of wt. loss (if any) is UNK

(25): ANCILLARY DATA

Certain significant para-clinical findings are coded here:

Anemia: Criteria are as follows:

Men: Hct. 37 or less; Hgb. 11.9 or less
Women: Hct. 34 or less; Hgb. 11.4 or less

If values for both hematocrit and hemoglobin are given, and only one is normal, use the hematocrit value for making the decision.

Elevated VP: Elevated venous pressure is coded when it is regarded as evidence of the SVC syndrome, particularly when this VP is the only significant evidence to indicate SVC. The measurement may have been performed in an arm vein or neck vein, and the criteria for coding or not coding it will depend on whether a therapeutic decision (radiotherapy, chemotherapy, or deliberately no therapy for SVC) was evoked by the result. If no clinical evidence of the SVC syndrome is coded in category 4 of column 19, and if the venous pressure evokes a therapeutic decision for SVC, then the elevated VP should be coded here. If no therapeutic decision is made about SVC, do not code here. If clinical evidence of SVC is present, and the syndrome receives a therapeutic decision, record the elevated VP if it is abnormal according to ad hoc criteria.

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Hypercalcemia or Other: This category is used to denote unusual or striking para-clinical evidence of tumor effects in the absence of associated codable clinical signs and symptoms. In addition to hypercalcemia, the findings to be coded here include: X-ray evidence of HPO; laboratory data suggesting abnormal ADH secretion; para-clinical tests suggesting metastasis, such as strikingly abnormal liver function studies; and a laryngoscopic finding of "poorly moving vocal cord" in a patient who is not hoarse. By convention, thrombophlebitis believed due to cancer is also coded here.

(26): SPUTUM CYTOLOGY; MEDIASTINOSCOPY

These two unrelated entities are cited together here solely for purposes of compactness in coding. A sputum cytology reading of "saliva, inadequate specimen" is regarded as "unknown" for this coding.

If no mediastinoscopy was performed or if no tumor was grossly visualized at mediastinoscopy, code sputum cytology as:

- 0: None positive
- 1: None positive; at least one equivocal
(includes "atypical" and "dyskeratotic")
- 2: Only one positive
- 3: Two or more positive
- 4: UNK or not done

If tumor was grossly visualized at mediastinoscopy, code sputum cytology as:

- 5: None positive
- 6: None positive; at least one equivocal
(includes "atypical" and "dyskeratotic")
- 7: Only one positive
- 8: Two or more positive
- 9: UNK or not done

Note: If tumor was grossly visualized at mediastinoscopy, and microscopic specimens were not obtained or were read as negative for tumor, code gross visualization as 81 in columns 34-35. (See Microscopic Classifications, Appendix D.)

(27): GROSS PLEURAL FLUID

Categories 3, 5, and 9 of this column are significant in coding the Anatomic Group (Appendix F). Categories 1 - 8 refer to ipsilateral effusions; if a lateral primary site of the cancer is not specified, or if the extractor failed to note the side of the effusion, assume that the effusion is ipsilateral. If one specimen is bloody and another is sero-sanguinous or pink, code the one that was removed earliest. If one specimen is normal in appearance and another contains blood, code the bloody specimen.

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- 0: None noted or no thoracentesis performed
- 1: Pleural fluid was noted at physical examination, or was of "major proportions" (see criteria for "major proportions" in column 40) in the pre-zero X-ray, but no thoracentesis was performed. This designation can be used to separate patients with Pancoast tumor alone (coded as 1 in column 40) from patients with pleural effusion (also coded as 1 in column 40), if the existence of pleural fluid is not coded elsewhere in this column
- 2: "Amber", "serous", or "normal" in appearance
- 3: First specimen sero-sanguinous or pink
- 4: Subsequent pre-zero specimen sero-sanguinous or pink
- 5: First specimen bloody
- 6: Subsequent pre-zero specimen bloody
- 7: Specimen removed but not described
- 8: Pleural fluid attributed to cause other than lung cancer. Fluid may or may not have been bloody
- 9: Contralateral first specimen pink, sero-sanguinous, or bloody

(28): RESPIRATORY RESERVE

Test Abnormal: The "test" used for most of the 1953-1964 case series is the MBC (Maximum Breathing Capacity), which is also called the MVV (Maximum Voluntary Ventilation). An abnormal MBC value is <50, expressed in liters per minute or in percentage. If MBC is recorded in both liters per minute and percentage, choose the value of liters per minute for coding this category. If the MBC was not recorded or was not used as the critical test of respiratory reserve, use values of "normal" and "abnormal" appropriate for the alternative test.

M.D. Statement re Poor Ventilation: This entity must be cited in the record by such phrases as "low respiratory reserve" or "poor ventilatory capacity".

Severe Dyspnea: This category is used for indicating unusually severe instances of dyspnea in which the dyspnea itself is life-threatening or has highly adverse prognostic connotations. The citations below indicate some, but not necessarily all, of the situations in which this category may be coded:

(a) The magnitude of the dyspnea is described in such phrases as: "extreme", "at rest", "on minimal effort", "marked respiratory distress", "sit up all night", "air hunger" or "choking". The term "severe", if not further specified, does not alone suffice for coding the category. In addition, the cited degree of severity should be present in the absence of pleuritic chest pain.

(b) Orthopnea, progressively worsening, within one month before admission, in the absence of pleuritic pain, CHF, or the SVC syndrome.

(c) A rapidly progressive worsening of dyspnea. Examples (not exhaustive) of such a rapid progression are at least two distinct transition points in the previous three months; or at least one transition point in the previous 3 weeks with continued worsening thereafter.

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Note: These categories are additive. A normal "test" (MBC > 50 liters per minute or percent) or the absence of data from such a test is coded as making a 0 contribution to this column.

(29) - (30): BRONCHOSCOPY REPORT

(29): BRONCHOSCOPY FINDINGS

- 0: Negative findings for mass
- 1: Mass in or above carina
- 2: Mass in carina and at least one main bronchus
- 3: Mass in main bronchus, close to carina
- 4: Mass in main bronchus, not otherwise specified
- 5: Mass in main bronchus, at distance from carina
- 6: Mass in a lobar bronchus, not in main bronchus, i.e., RULB, LLLB, etc.
- 7: Not done or UNK

Note: If tumor was grossly visualized at endoscopy, and microscopic specimens were not obtained, or were read as negative for tumor, code gross visualization as 81 in columns 34-35. (See Microscopic Classifications, Appendix D.)

(30): BRONCHOPATHOLOGY OR LUNG BIOPSY

- 0: Test(s) done; none positive
- 1: Positive biopsy and cytology
- 2: Positive biopsy; cytology not positive, but done
- 3: Positive biopsy; cytology not done
- 4: Biopsy not done; cytology positive
- 5: Biopsy not positive; cytology positive
- 6: Positive lung biopsy
- 7: No tests done or tests unsatisfactory

(31): CLINICAL ANATOMIC EVIDENCE

This section is used for unequivocal anatomic evidence of metastasis, noted as physical signs by the examining physicians. If the manifestations were also noted by the patient, they are coded in column 20 or 21 as appropriate.

Palpable Thoracic Metastasis: This category refers to metastases that are palpable in the outer thoracic coverings of bones and chest wall. Intracutaneous or subcutaneous nodules in the thoracic region may be coded here if contiguously attached to underlying structures such as rib, or thoracic muscle; if not contiguous, these are coded as ultrathoracic in the next category below. Parathoracic nodes are coded here if they are considered to be involved with cancer, regardless of their contiguity. When a palpable thoracic metastasis is considered contiguous with the underlying primary, its contiguity is coded in column 32. When such a palpable metastasis is contralateral to the primary, its contralaterality is indicated in column 33.

Palpable Surface Metastasis: The acceptable topographic sites are those noted in Appendix B as ultrathoracic, and the acceptable manifestations are intracutaneous, subcutaneous, and/or large lymph node masses, nodules,

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or lumps regarded as CA metastases. For palpable masses in the thoracic region to be coded here, such masses must be described as "cutaneous" or "subcutaneous", and evidence of non-contiguity must be present.

Liver or Other: A palpated liver can be regarded as involved with tumor if, in the absence of alternative explanations for hepatomegaly, one or more of the following conditions are fulfilled: (a) the liver is found to be "markedly enlarged" by X-ray; (b) the liver is palpated to be "hard" and "nodular", with distinct "large" nodules outlined; or (c) the liver is palpated as "hard" or "firm", and at least 10 cm. (5 finger-breadths) below the costal margin. The term "other" refers to non-hepatic anatomic evidence of metastasis, such as large masses observed by the physician on deep palpation of the abdomen or pelvis.

(32) - (33): EXTRAPULMONIC MORPHOLOGIC EVIDENCE

These two columns are used primarily to record visible morphologic evidence obtained from sites other than the bronchus or pulmonary parenchyma. The evidence can be microscopic (histologic or cytologic) or a gross anatomic description of tumor observed during endoscopy or surgical exploration. The categories are arranged to record site, contiguity, and laterality of the evidence. The categories for contiguity and laterality are used to describe the morphologic evidence coded in this column, and also any palpable thoracic metastases coded in column 31. Criteria for contiguity and laterality are described in Appendix B.

If "metastatic surgery" was performed before or at zero time, consult Appendix G for decisions about coding it in these columns.

(32):

Regional Node: Record positive morphologic evidence from a parathoracic node, regardless of its location, and/or positive morphologic evidence from mediastinal nodes.

Pleura, Pleural Fluid, Chest Wall or Thoracic Bone: Includes positive evidence from any of these sites. Skin or subcutaneous tissue is considered as "chest wall" if contiguous to an underlying lesion, and as ultrathoracic if not contiguous. "Thoracic bone" includes both the endothoracic and perithoracic bones.

Contiguous Involvement: This category is used to "reduce" the extensiveness of peripulmonic and perithoracic involvement when involved structures are contiguous with the underlying primary lesion. (See Appendix B for a complete discussion of contiguity, and enumeration of perithoracic and peripulmonic structures.) This category refers to all morphologic evidence (except pleural fluid cytology), coded in categories 1 and 2 of column 32, and to the clinical anatomic evidence cited as "palpable thoracic metastases" (1 in column 31). Code 4 in column 32 if all of the positive entities cited in category 1 of column 31 and categories 1 and 2 of column 32 are contiguous with the underlying primary lesion. If any of the positive entities is not contiguous, do not code category 4. Mediastinal nodes, by convention (see Appendix B), are always considered contiguous unless the primary is clearly shown to be located in

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the periphery and to be contiguously involved with peripheral structures. A pleural or parathoracic node biopsy would not be considered contiguous unless the primary were clearly peripheral, and adjacent to the biopsy site.

(33):

Pericardial Involvement: This category refers to microscopic evidence from the pericardium or from pericardial fluid. Its contiguity need not be determined.

Contralateral Site: Code this category for contralateral involvement of any one of the entities coded in category 1 of column 31 or categories 1 or 2 of column 32. Mediastinal nodes are considered ipsilateral unless they are specifically noted to be contralateral.

Ultrathoracic Site: This category refers to all extrathoracic locations. Brain and extrathoracic spinal cord, when involved, are cited in column 76 as well as here. In addition to CNS structures, the sites to be coded here include: skull, liver, cervical node, non-thoracic bone, extrathoracic cutaneous mass, and non-contiguous subcutaneous thoracic masses.

(34) - (35): PRE-TREATMENT MICROSCOPY

Use the Designation of Cell Types listed in Appendix D. If the same slide has received several positive histologic readings, choose the one closest to, but before, zero time, or the one that was regarded as the cell type at zero time.

If Histologic Discrepancy exists among the readings at several sites, or if Histologic Disparity exists among several readings of same slide, code in column 73. Use Appendix D to determine when two histologic readings are inconsistent enough to be called a discrepancy or disparity.

(36) - (42): RADIOGRAPHIC INTERPRETATIONS

(36): RADIOGRAPHIC DESCRIPTION

The object of this category is to indicate situations in which the X-ray diagnosis at zero time was erroneous, either by omission or commission.

In categories 1, 2, and 3 the gross X-ray at zero time was originally read as negative. In category 1, the "error" was never rectified, and the film, if later reviewed, was still regarded as negative. In category 2, the film was later reviewed after zero time (when a lung cancer had been identified at thoracotomy, necropsy, or by other means) and the positive finding was noted retrospectively. In category 3, a positive pre-zero diagnosis was established only by laminography or by radiographic methods other than the standard X-ray.

In categories 5, 6, and 7, the error was one of commission: a lesion was noted at roentgenography, but was regarded and initially managed as something other than lung cancer. In all three of these situations, the discovery of the error took place after zero time, i.e., at thoracotomy, necropsy, or during the extraction and coding procedures.

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The codes are:

- 0: No chest X-ray taken [may occur in our "necropsy detection" cases]
- 1: Negative X-ray. Even in retrospect, no abnormalities were noted
- 2: X-ray positive, in retrospect; diagnosis of 1° CA lung not made before zero time
- 3: Gross X-ray negative or equivocal; laminograms or other radiographic methods positive
- 4: X-ray definitely positive, by exclusion
- 5: X-ray positive; read, until after zero time, as TBC
- 6: X-ray positive; read, until after zero time, as primary intrathoracic lesion, such as non-tuberculous inflammatory disease, degenerative disease, benign neoplasm, or Hodgkin's disease
- 7: X-ray positive; read, until after zero time, as metastatic to lung, not 1°

(37) - (38): RADIOGRAPHIC LOCALIZATION

These columns are used for indicating the site of the primary tumor. There are two locations to be cited: a lateral side and a vertical site. The vertical site should be decided upon first, because its description determines the digit used for coding the lateral side.

If intrathoracic metastases exist, their sites are coded in column 40 or 41. Examples and further comments about X-ray coding are presented in Appendix E.

Note: If chest X-ray was not taken or was negative for cancer (i.e., no lesion seen before zero time), use columns 37-38 to code location of the tumor according to the site subsequently discovered in other ways. Order of choice: (a) pre-zero bronchoscopy; (b) any other pre-zero reading; (c) surgery; (d) post-zero X-ray; (e) necropsy.

(37): PRIMARY SIDE

- 0: Not applicable [X-ray negative or not taken, and no other suitable data available]
- 1: R. lung, next digit is Lobe
- 2: L. lung, next digit is Lobe
- 3: R. lung, next digit is Field
- 4: L. lung, next digit is Field
- 5: Mediastinum only. The next digit should be 0
- 7: Both sides involved; or primary side not specifiable.
The next digit should be 0

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(38): VERTICAL LOCATION

Lobe Code

0: Not applicable or UNK§
1: Upper†
2: Middle (or Lingula†)
3: Upper and Middle
4: Lower
5: Upper and Lower
6: Middle and Lower
7: All 3 lobes

Field Code

0: Not applicable or UNK§
1: Upper
2: Middle
3: Hilum or Mediastinum¶
4: Lower
5: Vertical site not specified;
or not specifiable for reasons
other than those cited in 6
and 7
6: Lung obscured by massive
opacity
7: Atelectasis of all 3 lobes
8: Main bronchus

(39): MEDIASTINAL INVOLVEMENT

Definite Hilar Nodes: This refers to involvement of the hilum or hilar nodes on the same side as the primary lateral side. If no primary lateral side has been identified, and a lateral hilum is involved, code here. If hilum is involved on the other side, code in column 41. If the patient has "bilateral hilar involvement", code here and also in column 41. Do not code if the involvement is marked minimal, questionable, dubious, or uncertain.

Anatomically, the hilum is a part of the mediastinum, but in the designation here and in most X-ray reports, the term "mediastinum" refers either to central mediastinal regions that cannot be lateralized to a particular hilum, or to superior mediastinal regions located above the hilum. Accordingly, the category hilar nodes is not coded if the report is only "mediastinal involvement", nor is the latter category coded only on the basis of "hilar involvement".

If a tumor is marked as arising in a hilum and as involving an adjacent lobe or field of the lung, code that lobe or field in columns 37-38, and code the hilum here. See Appendix E for examples of this type of situation.

§ = Neg. X-ray, or 0, 5, or 7 in column 37.

† = According to the anatomic circumstances described by the radiologist, the lingula can be coded separately as a type of "middle" lobe, or it can be included as part of the left upper lobe.

¶ = To avoid losing information, use this entry only when no other vertical site appears involved. If the tumor "arises in hilum" and appears to involve a distinct vertical site on one side, code that vertical site in column 38, and code the hilar "origin" in column 39.

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The following terms indicate the topographic location of the hilum: hilum, hilus, hilar, or any of these terms prefixed by peri- or para-. The following terms will indicate involvement at this topographic site: originates, arises, extends from, prominent, involved, enlarged, widened, adenopathy.

Definite Mediastinal Nodes: The following terms indicate the topographic location of "mediastinum": mediastinum; mediastinal; or any of these two terms prefixed by, or associated with, para-, peri-, near supra- or superior; para-tracheal; peri-tracheal; tracheal. The following terms indicate involvement of lymph nodes in this topographic location: involvement, enlarged, widened, adenopathy. Do not code if the involvement is cited as minimal, questionable, dubious, or uncertain, or if the "widening of the mediastinum" is attributed to vascular or other non-neoplastic causes.

Do not code this category if the mediastinum is reported as "shifted" or "displaced" without a specific statement of involvement by tumor. In these situations, there should be a pleural effusion, atelectasis, or other explanation for the shift of the mediastinum.

Mediastinal "Viscera": This designation refers to the specific structures topographically designated by the terms: pericardium; esophagus; trachea; diaphragm; and the large mediastinal blood vessels -- aorta, pulmonary artery, and pulmonary veins. Do not code any structure whose involvement is minimal, questionable, uncertain, or dubious. The following descriptions will indicate involvement of these topographic sites:

Pericardium: Involved or effusion, without evidence of non-neoplastic cause.

Esophagus: Involved, displaced, impinged upon, or narrowed, without evidence of non-neoplastic cause.

Trachea: Involved or displaced; and not attributed to atelectasis, pleural effusion, or causes other than neoplastic nodes or direct neoplastic involvement.

Diaphragm: Involved, paralyzed, or elevated. The word "paralyzed" requires appropriate evidence either from fluoroscopy or from films taken in inspiration and expiration. The word "elevated" requires a significant amount of elevation, and not just "slight". In any of these situations, the diaphragmatic involvement should be caused by an intrathoracic cause (rather than an intra-abdominal cause, such as ascites or a large liver); and the intrathoracic cause should not be attributable to atelectasis, or old inflammatory adhesions (often cited as "tenting").

Mediastinal Vessels: The involvement will usually be demonstrated by angiography.

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(40): IPSILATERAL THORACIC INVOLVEMENT

Do not code questionable involvement of any of the structures cited here. If any of the structures in this section is involved by a tumor that cannot be lateralized, the involvement should be coded here. (See Appendixes B and E for further discussion and examples of coding.)

Pancoast Tumor or Pleural Effusion: Although coded here when appropriate, neither of these entities is used for the "staging" of Anatomic Groups. "Pancoast tumor" is omitted because the term is not applied with topographic specificity in radiographic reports. (The involvement of bone or chest wall by such a lesion, however, is considered for anatomic staging, and is cited in categories 2 and 4 of this column.) "Pleural effusion" is omitted from anatomic staging because this roentgenographic designation cannot alone provide adequate evidence that the effusion is neoplastic. A pleural effusion is considered in anatomic staging, however, if it is bloody (cited in column 27), or if microscopic evidence shows it to be neoplastic (cited in column 32). The following specifications are used for these two entities:

Pancoast Tumor: Sometimes called "superior sulcus tumor". This tumor is located at the apex of the lung, and is characterized by its anatomic invasion of bone, chest wall, or neural structures. The invasion is manifested by roentgenographic evidence, or by clinical evidence of the types cited in column 20, and must be cited by name to be coded here.

Pleural Effusion: Code when the effusion is of major proportions. A "major proportion" is of magnitude great enough to obscure the lung roentgenographically; or to create respiratory distress; or to evoke a therapeutic (rather than purely diagnostic) thoracentesis; or that yields 1000 ml. or more on thoracentesis; or that is cited as "large" or "moderately large". Do not code if the effusion is reported as "small", "minimal", or "confined to the costo-phrenic sulcus". Whenever an effusion is coded here, an appropriate positive entry should be made in column 27, so that Pancoast tumors can be separated from pleural effusions during data retrieval.

Peripheral Primary or Contiguous Involvement: This category can be used for two different purposes. It can denote that a localized tumor has a peripheral location or "coin"-like appearance; alternatively, this category can be used to "diminish" the "isothoracic" category, below, by indicating that the cited involvement there was contiguous to an underlying parenchymal tumor. Radiographic reports should usually state "peripheral" or "coin" lesion for "peripheral primary" to be coded here.

If "isothoracic structure(s)" is coded in the next category below, a code here will mean that all of those structures were involved contiguously. If any one of them was involved non-contiguously, do not code here. This "peripheral primary" category will denote a peripheral primary or coin lesion only if the "isothoracic structure" category is not coded. (A brief recapitulation of the use of these two categories appears after the discussion of the "isothoracic" category.)

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Isothoracic Structures: The topographic sites to be coded here are any one or more of the following:

Pleura: When reported as "involved", usually because nodules are seen after removal of a pleural effusion. The effusion itself is not coded here.

Chest Bones: These include the scapula, clavicle, sternum, ribs, and thoracic vertebrae. Code only when one or more of these were reported as definitely, not questionably, involved on the X-ray.

Chest Wall: When soft tissue involvement is shown on X-ray; clinical evidence is coded elsewhere in columns 20 and 31.

Spinal Cord: Myelographic demonstration of a mass in the thoracic region.

Distant Parts of Lung: When two different parts of the lung are involved on the same side and the involvement is anatomically disconnected. This citation will be uncommon, because the involvement of several lobes is ordinarily contiguous, and will be cited appropriately in column 38.

Thus, if "peripheral" is marked present, and "isothoracic" is not, the result means that the patient has a localized peripheral or "coin lesion" tumor. If "isothoracic" is marked present and "peripheral" is not, the result means that the patient has non-contiguous involvement of one or more of these isothoracic structures. If "peripheral" and "isothoracic" are both marked present, the result means that one or more "isothoracic" structures are involved, and that all of them are involved contiguously.

(41): CONTRALATERAL THORACIC INVOLVEMENT

Questionable Involvement or Pleural Effusion: Use this code when a primary side has been identified, and when any contralateral structure has been cited as having questionable involvement. This category is also coded when a contralateral pleural effusion has been reported. Except for topography, the pleural effusion is cited here according to the same criteria noted in category 1 of column 40.

Hilum or Mediastinum: Code when there is bilateral involvement of these structures, or specific involvement of the contralateral hilum or mediastinum.

Other Contralateral Structures: Code when there is involvement, other than hilar or mediastinal nodes, of any definite structure on the other side. The candidate structures are lung, pleura (when cited as "involved"), bones, chest wall, and thoracic cutaneous tissue that is contiguous to an underlying lesion.

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(42): ULTRATHORACIC INVOLVEMENT

Extrathoracic Bone: Skull, pelvis, long bone, non-thoracic vertebra.

Liver or Abdominal Mass: Large liver, abdominal mass, other non-CNS extrathoracic evidence.

Other: This category really refers to CNS lesions, such as mass on ventriculography or extrathoracic myelography; pineal shift. Other non-thoracic but non-CNS sites should be coded in either of the two foregoing categories.

(43): ANATOMIC GROUP

This is an arbitrary coding system developed for this research, and based on the topographic extent of the radiographic, microscopic, and gross anatomic evidence of cancer available at zero time. Criteria for topographic classification are listed in Appendix B. Criteria for the categories listed below are found in Appendix F.

- 1: "Endopulmonic"
- 2: "Vicinal"
- 3: "Isothoracic"
- 4: "Contrathoracic"
- 5: "Ultrathoracic"
- 6: UNK

(44): ADDITIONAL PROGNOSTIC CO-MORBIDITY

This column is used to cite prognostically significant conditions not indicated in the preceding columns. A condition or associated ailment is regarded as prognostically significant if it is expected to have a more unfavorable effect on the outcome of the clinical course than is otherwise anticipated. The "associated phenomena" considered here can be unusually severe functional effects of the cancer itself, or the effects of separate co-morbid diseases. Since prognosis is customarily based on length of survival, the designation of "prognostic co-morbidity" is used mainly for conditions that can be expected to impair life expectancy.

The cancer itself may be regarded as having severe functional effects when it has caused the patient's actual clinical state to be substantially worse than that of other patients with comparable anatomic dissemination and with the same general clinical phenomena. For example, consider two patients who both have the same primary symptoms and who both have weight loss and fatigue as the only systemic symptoms. One of these patients may be ambulatory and otherwise in good health, whereas the other patient may be cachectic and bed-ridden. As another example, two patients may both have clinical evidence of cerebral metastasis, but one patient may have hemiplegia as his only manifestation, whereas the other may be obtunded or comatose. In both of these examples, the pairs of patients are classified in the same general clinical and anatomic groups, but the second patient in each pair was more severely ill and had a significantly worse prognosis than the first.

Regardless of whether an "associated ailment" is attributed to functional effects of the cancer, or to a co-morbid disease (or to both), decisions about prognostic co-morbidity are difficult. Research of the type described in this coder's manual is intended to quantify the prognosis of lung cancer, but such research has not yet been performed for the many co-morbid ailments encountered in patients with lung cancer. Consequently, decisions about prognostic co-morbidity

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must be made as a matter of careful clinical judgment. The judgment entails consideration of both the prognostic import and the diagnostic attribution of each of the candidate phenomena. To establish precedents, maintain consistency, and develop specific criteria for making these decisions, a "running log" should be kept of all such decisions, recording the salient data and reasons for each decision.

Certain situations encountered in medical records can be immediately regarded as evidence of prognostic co-morbidity. Such situations include the following:

(a) Statement by the attending M.D. that the patient had a life-threatening co-morbid disease or that the cancer in this particular case carried an exceptionally poor prognosis.

(b) The patient's condition was bad enough to prevent a suitable diagnostic work-up for the cancer.

(c) The "associated ailment" was severe enough to prevent a decision about anti-neoplastic therapy. The absence of an anti-neoplastic therapeutic decision need not be due, however, to overt co-morbidity. The patient may have died suddenly or unexpectedly (category 2 in column 60), or a therapeutic decision may not have been made only because the primary site of the cancer was unknown; such instances are not coded as prognostic co-morbidity.

Other situations encountered in medical records can often be interpreted as evidence of prognostic co-morbidity. In such situations, a co-morbid condition has been cited as the M.D.'s reason for rejecting a therapeutic agent (such as surgery) that might otherwise be desirable. The clinical judgment about such conditions is subtle. For example, multiple previous myocardial infarctions would be regarded as prognostically significant, although a single, temporally distant myocardial infarction would not. Congestive heart failure, if manifested by peripheral edema, is almost always prognostically significant, but may not be, if manifested only by dyspnea.

In many cases, a definite diagnostic attribution cannot be made for a prognostically significant condition. The condition may have been due to the cancer, to a co-morbid disease, or to both. We ascribe prognostic significance to a co-morbid disease only when the disease was diagnosed as definitely present and when the prognostically significant condition was attributable to the co-morbid disease. Thus, if the problem in attribution is that the condition might equally be due either to the cancer or to the co-morbid disease, the co-morbid disease would not be coded here. However, in the instances where the particular prognostic condition is regarded as caused by both the cancer and the co-morbid disease, then the co-morbid disease should be coded as well. Thus, if a condition is considered to be prognostically significant, the following principles may be used to decide the category for its coding here:

(a) If prognostically significant manifestations -- other than extreme weight loss or severe dyspnea -- have been coded in any of columns 12 through 21, code 1 in column 44. If any of these manifestations are conjunctively attributed to a definitely identified co-morbid disease(s) code 2 and/or 4 as appropriate in column 44.

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(b) If any remaining prognostically significant manifestations have not been coded in columns 12 through 21, and can be attributed exclusively to co-morbid disease(s), code the disease(s) appropriately as 2 and/or 4 in column 44.

Categories 1, 2, and 4 are further defined as follows:

Severity of Tumor Effects: Do not use for re-coding extreme weight loss (1, 2, or 3 in column 24) or severe dyspnea (4, 5, 6, or 7 in column 28). Use for coding any other symptom that has already been coded in columns 12 through 21, and that is regarded as prognostically significant. Among such effects are: rapidly progressive cerebral neurologic dysfunction; impairment of sensorium due to presumptive cerebral metastases; metastatic phenomena involving two or more distinctly different vital topographic regions; and dyspnea in association with a pleural effusion so large that no localizing vertical lesion is discernible on the initial (pre-thoracentesis) X-ray of the chest.

Significant Cardiovascular Disease: With the prognostic and attribution qualifications cited earlier, this category may include such entities as: stroke, other types of cerebrovascular accident, malignant hypertension, intractable angina pectoris, severe congestive heart failure, and multiple past episodes of myocardial infarction.

Other Co-Morbid Conditions: With the prognostic and attribution qualifications cited earlier, this category is coded for such conditions as advanced renal disease, intractable hepatic decompensation, severe or probably progressive neurologic damage, and acute leukemia.

In summary, a symptom, disease or condition that is judged to be prognostically significant is coded in column 44. If attributed or questionably attributed to the cancer, it is coded as 1. If exclusively or conjunctively attributed to a co-morbid disease, it is coded accordingly as 2 or 4.

(45) - (46): CONTRA-THERAPY REASONS

In most cases, the categories listed in these two columns are used to denote the reasons expressed for rejecting surgical therapy, although contra-indications for other therapy may also be cited. A reason such as "metastasis of tumor" can sometimes be inferred as the contra-surgery reason even if it is not specifically recorded. A citation of "metastasis" may also be marked here, even though the suspected lesion is coded only as 4 in column 22.

A special use of these columns is for situations in which a surgical resection was performed, but was deliberately limited in scope (such as lobectomy rather than a preferred pneumonectomy) because of "low respiratory reserve" or some other reason. If thoracotomy was performed as a "subsequent" treatment (i.e., 1 in column 54 rather than 4 in either of column 47 or 48), the reasons for deferment of surgery must be cited here, unless due to patient's initial refusal. If the M.D. made a decision for "no treatment" (i.e., 1 in column 47), a contra-therapy reason must be coded in one of these two columns. If a patient is too sick for work-up, these two columns are not coded; such a patient should be coded in column 44. If no decision was made regarding treatment, these columns should not be coded.

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The contra-therapy reasons are divided into "oncogenic" ones that are directly or probably related to cancer, and "non-oncogenic" ones that have other origins. This separation is somewhat arbitrary, and used mainly for convenience in classification.

Of the oncogenic categories cited in column 45, the first two are clearly associated with the cancer. The third can be coded if unusually severe symptoms, coded in columns 12-21, were cited as a contra-therapy reason.

Note: Entries coded in columns 45 and 46 need not always be prognostically "significant". Such situations can occur when a patient appears to be in relatively good condition despite an anatomic metastasis or a co-morbid disease (such as recent myocardial infarction) that may be regarded as contra-indication to therapy.

(45): ONCOGENIC

Juxta-Carinal or Cell Type: These two unrelated entities are coded together here solely for convenience in format.

Juxta-Carinal: Refers to circumstances in which pulmonary resection is regarded as technically unfeasible because the tumor is located in or near the carina, or because the main bronchi are involved by adjacent hilar or mediastinal nodes.

Cell Type: Refers to circumstances in which surgery was rejected because the "tumor is too anaplastic" or when "insensitive cell type" was cited as a contra-radiation reason. This category may also be coded if a mode of treatment was contra-indicated by lack of microscopic evidence of cancer.

Metastasis of Tumor: Refers to any clinical or anatomic manifestation indicating metastasis or spread of the cancer, or M.D. statement that suspicion of metastasis prevented therapy.

Functional Severity of Tumor Effects: To be coded when the unusually severe effect of a particular symptom(s) or the adverse systemic effect of the tumor is cited as the contra-therapy reason. This entry may also be used when a local anatomic effect, such as a pulmonary abscess, is used as a surgical contra-indication.

(46): NON-ONCOGENIC

Low Respiratory Reserve: Code whenever this condition has been cited as a contra-therapy reason. The condition may have been described by a suitable entry in column 28, or in such alternate phrases as "poor ventilatory capacity", "impaired pulmonary function", or "severe dyspnea". If the condition is due to an associated pulmonary disease, the functional effect of that disease will be adequately noted here and the disease should not be coded as "co-morbid disease" in the next category of this column.

Co-Morbid Disease: Code whenever a co-morbid disease has been cited as a contra-therapy reason, with the exception of solitary dyspnea, as just

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noted. "Poor nutrition", if not due to effects of the cancer, is regarded as a co-morbid disease.

Other: This category includes such "non-disease" entities as age and obesity. The category may also denote a situation in which the cancer was untreated because the primary site was unknown or a definitive diagnosis was not established. Whenever this category is used, the coder should record the specific reason on the coding form itself.

(47) - (48): THERAPEUTIC PROCEDURAL DECISIONS

The coding here depends on the sequence in which treatment was actually given, regardless of the therapeutic event chosen to be zero time, as described in Appendix A. Conventions for coding metastatic surgery are provided in Appendix G.

Another coding convention deals with "paired treatment", which refers to two (or more) different therapeutic agents chosen on the basis of evidence describing a single clinico-anatomic state. The agents are planned to be delivered sequentially or concomitantly without any intervening change in the patient's condition. Examples:

(a) At thoracotomy, decision is made to follow the surgery with radiation to the primary site. In this pair, surgery is the first element and radiation, the second. If the thoracotomy were followed by both radiation and nitrogen mustard, the second element of the pair is the doublet of primary radiation and cytotoxic.

(b) At bronchoscopy, tumor is judged too close to carina. Decision is made to irradiate and then do surgery. If the surgery is performed regardless of post-irradiation effects, it is the second element of the pair. If the mediastinal nodes or other manifestations must regress in order for the surgery to be done, it is a separate second course of therapy, not a paired part of the first course.

(47): FIRST THERAPEUTIC ACTION

If the first anti-neoplastic treatment cited in column 47 was an alternative to a previously refused agent, the patient's previous refusal is coded with 2 in column 48; if the previously offered treatment was thoracotomy, it is also coded as 8 in column 49. If a paired treatment was planned to follow the treatment coded in column 47 but was not given, code 3 in column 48 and, if appropriate, 8 in column 49. If 4-9 is coded in column 47, a 4-9 in column 48 indicates paired therapy. If 2 or 3 is coded in column 47, a 4-9 in column 48 indicates the treatment that was planned or offered, but not given.

In a patient who has received no anti-neoplastic treatment, the medical record may not contain a specific statement that clearly indicates whether 0 or 1 should be coded in this column. The type of decision is often implied, however, by clues in the pattern of events. Thus, if microscopic evidence of cancer was obtained at a time when the patient was not obviously moribund, the doctors probably decided not to treat. On the other hand, if the diagnosis of cancer was never established, or if microscopic evidence had not been obtained, it is likely that no therapeutic decision was made by the doctors.

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- 0: No treatment. No decision made by M.D. re treatment (patient died too soon, or was a necropsy surprise, or work-up was incomplete)
- 1: No treatment. M.D. made decision to give no anti-neoplastic treatment
- 2: No treatment. Patient refused to accept anti-neoplastic treatment offered by M.D. [Code the offered treatment in column 48]
- 3: No treatment. M.D. planned to give anti-neoplastic treatment but the plan was not carried out for reasons other than patient refusal. [Code the planned treatment in column 48]
- 4: Thoracotomy
- 5: Primary radiation (to lung and/or mediastinum)
- 6: Cytotoxic (includes HN₂, systemic radio-isotopes, TEM, 5 FU, etc. Does not include antibiotics, narcotics, sedatives, etc.)
- 7: Primary radiation and cytotoxic
- 8: Radiation to metastatic site (includes intrapleural radiotherapy)
- 9: Local treatment of metastatic site, with surgery or cytotoxic therapy (for the coding of metastatic surgery as opposed to metastatic biopsy as zero time events, see Appendix A)

(48): OTHER THERAPEUTIC CONSIDERATIONS

- 0: None (no paired treatment, or not applicable)
- 1: Patient refused diagnostic work-up
- 2: Patient refused M.D.'s first therapeutic offer, but accepted and received the alternative treatment coded in column 47
- 3: A paired treatment was planned to follow the treatment coded in column 47, but was not given because patient refused, his condition changed, or he died too soon. If the planned paired agent was thoracotomy, code 8 in column 49
- 4: Thoracotomy
- 5: Primary radiation (as specified in column 47)
- 6: Cytotoxic (as specified in column 47)
- 7: Primary radiation and cytotoxic
- 8: Radiation to metastatic site (as specified in column 47)
- 9: Local treatment of metastatic site (as specified in column 47)

(49) - (53): SURGERY

Columns 49-53 are coded whenever thoracotomy is performed, regardless of when it occurred in the sequence of therapy. If two thoracotomies were performed, use these columns for the thoracotomy that first removed the main tumor. If thoracotomy was not performed, category 4 of column 50 and columns 51-52 may be used to describe metastatic surgery.

(49): SURGICAL PROCEDURE AND INTENT

If the patient previously refused thoracotomy but later accepted it, disregard the earlier refusal in coding column 49.

"Palliative" is used here if this purpose was evident before or during the operation. Removal of the lingula alone is coded as a lobectomy. Removal of lingula and another lobe is coded as bilobectomy.

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- 0: Not applicable (no surgery to lung)
- 1: Thoracotomy; no excision of main tumor
- 2: "Palliative"; lobectomy or less
- 3: "Palliative"; bilobectomy
- 4: "Palliative"; pneumonectomy
- 5: No statement that surgery was "palliative"; lobectomy or less
- 6: No statement that surgery was "palliative"; bilobectomy
- 7: No statement that surgery was "palliative"; pneumonectomy
- 8: Patient was offered thoracotomy, but refused; or planned thoracotomy was not performed for reasons other than patient refusal

(50): FURTHER SURGICAL DESCRIPTION

Except for category 4, which might be based on surgery to a metastatic site, this column is coded for the surgical procedure noted in column 49.

Other Structures Excised, or Involved but 1° not Excised: The topographic sites coded as "other structures" are: pericardium, major vessels, and such chest wall structures as parietal pleura, ribs, and muscle. Mediastinal or hilar lymph nodes, and visceral pleura are not "other structures". Code as 1 if any of these structures were excised, or if any of these structures were noted to be grossly involved in a patient who had no excision of the main tumor. Do not code if these structures were involved but not excised in a patient whose main tumor was excised.

Post-op. Complications: A "complication" consists of dehiscence, wound infection, or major surgical difficulties. A major intra-operative problem, such as a period of cardiac arrest, can also be coded here.

Op. or Post-op. Death: The "post-operative" period ends when the patient is either discharged or transferred, for care of some other problem, to another service in the hospital. (E.G. Two days after surgery, patient becomes comatose; he dies after remaining in this state for two months. This situation is coded as a post-operative death.) If thoracotomy is not performed, this category can be used to code post-operative death after surgery to a metastasis. An "intra-operative" death (during operation or in the operating room) is coded as "sudden" in category 2 of column 60. Post-operative deaths may or may not be "sudden", according to the sequence of events. See further remarks in column (60).

If surgery has not been performed, this category may be used to code a "diagnostic death", occurring after bronchoscopy, liver biopsy, or some other procedure in the diagnostic work-up.

(51) - (52): SURGICAL HISTOLOGY

Use Designation of Cell Types listed in Appendix D.

Ignore readings of frozen sections, unless they provide the only positive histologic evidence.

If several readings are available for a slide, choose the initial reading for

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the slide, or the one on which a post-therapeutic decision was based. If subsequent review produced a disparate reading, code 4 in column 73.

(53): SURGICAL PATHOLOGY

This column contains a combination of the surgeon's report of gross neoplastic "spread" to lymph nodes or other structures beyond the pulmonary parenchyma, and the pathologist's microscopic findings of tumor extent. For the purposes of this column, the term "spread" is not applied to a surgical report of metastasis to another part of the same lung, or a microscopic reading of lymphatic or blood vessel invasion within an excised lobe. If no thoracotomy was performed, code 0; for all other situations except category 1, we assume that the surgeon either saw or palpated primary tumor. The codes are:

- 0: Not applicable, no thoracotomy performed; or surgeon reports no spread to lymph nodes or other structures; pathology report is unknown (nodes and other structures not removed or removed but not reported).
- 1: No tumor of any type (primary or beyond primary) noted at surgery.
- 2: Surgeon reports no spread to lymph nodes or other structures. Pathologist reports nodes negative, other structures negative or not examined.
- 3: Surgeon reports spread to lymph nodes and/or other structures. Pathology report is unknown (nodes and other structures not removed, or removed but not reported).
- 4: Surgeon reports spread to lymph nodes and/or other structures. Pathologist reports nodes negative, other structures negative or not examined.
- 5: Surgeon reports spread to lymph nodes only, no spread to other structures. Pathologist reports only one node positive, other structures negative or not examined.
- 6: Surgeon reports spread to other structures; lymph nodes may be grossly positive, negative or not mentioned. Pathologist reports only one node positive, other structures negative or not examined.
- 7: Surgeon reports spread to lymph nodes only, no spread to other structures. Pathologist reports more than one lymph node positive (or unspecified number positive), other structures negative or not examined.
- 8: Surgeon reports spread to other structures; lymph nodes may be grossly positive, negative or not mentioned. Pathologist reports more than one node positive, other structures negative or not mentioned.
- 9: Surgeon's report re spread may be positive or negative. Pathologist reports spread to other structures, lymph nodes may be positive, negative or not reported.

(54): SUBSEQUENT TREATMENT

This column is intended to record all of the modes of anti-neoplastic treatment that were given after the first course of treatment, regardless of the sequence in which these agents were given.

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Surgery to Primary Site: This category refers to an exploratory thoracotomy, with or without resection. In the therapeutic sequence of primary radiotherapy followed by thoracotomy, note the distinction, listed in column 47, that demarcates a "paired" sequence from two individual courses of treatment. If primary surgery occurs as a "subsequent" treatment, mark this category; then code the surgical procedure in column 49, its further description in column 50, and its histologic findings and pathology in columns 51-53.

Radiation to Primary Site: "Primary" radiation refers to treatment directed at the pulmonary parenchyma or mediastinum, not pleura or ribs.

Systemic or Metastatic Treatment: This category includes: systemic or focal cytotoxic agents; radiation directed at ribs, pleura, or ultrathoracic structures; and such exploratory or excising surgical procedures as craniotomy and laminectomy, if a significant amount of tumor was removed.

(55) - (56): SUBSEQUENT CLINICAL EVIDENCE OF METASTASIS OR RECURRENCE

The three main categories in these two columns are identical in contents. They differ only in their attribution as being "certain" in column 55 and "uncertain" in column 56.

The distinction between a "certain" and "uncertain" diagnostic attribution for post-zero events requires the same type of diagnostic judgments used for appraising the attribution of pre-zero events, except that the post-zero judgments are further complicated by the following: (a) side effects of anti-neoplastic therapy (e.g., radiation esophagitis); (b) occurrence of events outside the index hospital; and (c) problems of differentiating events due to debilitated or terminal state from those due more directly to cancer or to an associated disease. No specific set of rules for these judgments can be stated briefly, and many of the decisions will be made on an ad hoc basis. A "running log" should be kept of these decisions so that precedents can be established, and consistency maintained in subsequent codings.

The remainder of this discussion will deal with toponymic distinctions in the three categories.

New Endopulmonic or Systemic Manifestations of Tumor: This category is used for noting certain types of evidence that cannot be cited in the morphologic categories of column 57. Among the entities are:

(a) Hemoptysis in a patient who has not had it before zero time, or who has it after conclusion of the post-operative period that followed resection of the primary tumor. If the hemoptysis appears to have been associated with a pneumonia, code as ?-attribution; if the pneumonia occurs at a non-neoplastic site, do not code the hemoptysis.

(b) Appearance of HPO or of paraneoplastic syndromes that had not been present before zero time. If the only evidence of a new paraneoplastic syndrome is para-clinical, without clinical manifestations, do not code here; code as Special Note in column 73.

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(c) Anatomic evidence of endopulmonic recurrence on the same side as that of a surgically-removed tumor; or anatomic evidence of metastases to other parts of the ipsilateral lung. Evidence obtained from biopsy, surgical exploration, endoscopy, or unequivocal roentgenography is coded as attribution certain. Evidence from cytology is coded as ?-attribution.

New Evid. of Thoracic Involvement: This category is used to denote new clinical manifestations that suggest the thoracic metastases described by the findings listed in columns 19 and 20, and in category 1 of column 31. A new manifestation is not cited here if a previous manifestation had already occurred in the same general region. Thus, the new appearance of hoarseness [NMVC] would not be cited here for a patient who previously had SVC syndrome without hoarseness, because both manifestations are "mediastinal"; on the other hand, the new appearance of a Horner's syndrome would be coded here for such a patient, because it is "regional".

Development of a post-zero pleural effusion in the absence of a pre-zero effusion is coded with a 2 in column 55 if the effusion is large or massive on X-ray or physical examination and is bloody or pink and/or the cytology is positive. Code 2 in column 56 if the effusion is massive or large on X-ray or physical examination, but is non-bloody and its cytology is negative. If the pleural fluid cytology is positive, also code 1 in column 57. The cytology may be coded in columns 58-59 if warranted.

New Evid. of Ultrathoracic Involvement: This category is used for new clinical manifestations that would be regarded as ultrathoracic, according to the list of entities cited in column 21 and in categories 2 and 4 of column 31. Each new manifestation coded here should be in an anatomic location in which such manifestations have not been previously coded. For example, if a patient with pre-zero headache and seizures, attributed to cerebral metastases, develops post-zero hemiparesis, also attributed to cerebral metastasis, the new event would not be coded here.

(57): SUBSEQUENT NEW MORPHOLOGIC EVIDENCE

This column is intended to cite positive post-zero morphologic evidence in locations where no positive evidence of cancer was found before zero time. Topographically, the locations are in sites other than the ipsilateral endopulmonic parenchyma. Anatomically, the evidence consists of biopsy, cytology, gross visualization of tumor at surgery, or an unequivocal roentgenographic reading. (A positive specimen in sputum bronchoscopic material, lung biopsy or other ipsilateral parenchymal morphology could be coded, if warranted, in columns 58-59.)

Isothoracic: Refers to midline structures (mediastinal nodes, pericardium, esophagus, sternum, thoracic vertebra); or ipsilateral endothoracic structures (pleura, chest wall, ribs); or ipsilateral perithoracic structures (scalene node, clavicle, etc.).

Note: A pleural effusion by X-ray or physical examination is not positive morphologic evidence unless microscopically demonstrated to be neoplastic.

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Contrathoracic: Refers to any neoplastically involved structure on the side of the chest opposite the primary. If a primary side has not been established, use category 1 for denoting involvement of midline or lateral thoracic structures.

Ultrathoracic: Refers to any structure outside the thorax or its coverings. The topographic sites are listed in column 42 and Appendix B.

(58) - (59): SUBSEQUENT MICROSCOPIC EVIDENCE

This column is intended to denote the most convincing microscopic evidence of cancer that was found after zero time, but before necropsy. The order of preference for specimens and for sites is listed in Appendix D.

(60): MODE OF DEATH

Circumstances Unknown: This category refers to a situation in which we do not have specific information about the terminal events in a patient who did not seem moribund in the last known follow-up examination. If we do not know whether the patient is dead or alive, do not code here; code as a 2 in column 69. In the criteria cited below, the word "advanced" refers to a situation in which the patient, when last examined, had evidence of disseminated cancer.

Criteria for Coding "Unknown" in (60)

PATIENT'S STATE WHEN LAST NOTED	TIME BETWEEN LATEST FOLLOW-UP DATE AND DATE OF DEATH	CIRCUMSTANCE
Not "Advanced"	Any	Unknown
"Advanced"	> 6 mos.	Unknown
"Advanced"	< 3 mos.	Not Unknown
"Advanced"	> 3 but < 6 mos.	Individual decisions

Sudden or Unexpected: This category refers to a situation in which the patient was not specifically moribund at a particular moment, and then, in the next moment, the patient was either dead, or entered into a continuous sequence of rapid, adverse events that ended in death. Examples: gunshot suicide; exsanguinating hemorrhage; "coronary"; "stroke"; "dropped dead"; sudden asphyxia. In addition to the situations just cited, any intra-operative death is coded here. A post-op. death may be also coded if the sequence was sudden and rapid. Because a patient is so vulnerable during the post-op. period, the "suddenness" must be particularly distinctive to be recorded here, whereas a somewhat slower course may be acceptable as "sudden" for a patient who is not in the post-operative period.

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Definitely or Probably not Due to CA Lung: This category is based on clinical, not necropsy, evidence; and the necropsy data should not be used for this decision, even if the decision is thereby erroneous. The most obvious kind of extraneous lethal cause is suicide or externally inflicted trauma. Other examples are an unequivocal myocardial infarction or a stroke (with a rapid onset and rapidly fatal resolution). If no data are available to describe the terminal events, the diagnosis recorded on the death certificate suggests an extraneous lethal cause if the recorded diagnosis indicates such a cause, while either omitting any mention of cancer, or citing the cancer in a minor position on the certificate.

(61): ASSOCIATED DISEASES

Coexistent Other Cancer: This category refers to any other primary cancer (including another separate primary cancer of the lung), that was identified at any time in the clinical course, including necropsy. Leukemia or other hematologic neoplasms are regarded as cancers, as are certain benign tumors so designated by the checker (e.g., neurofibroma), but basal cell cancer of the skin and Kaposi's sarcoma are not regarded as cancers.

Coexistent Tuberculosis: This category refers to the occurrence of a clinical episode of pulmonary tuberculosis, regardless of when it appeared in the clinical course: before the "present illness", during the "present illness", or in the post-zero interval. If evidence was obtained to demonstrate that the diagnosis of TBC was fallacious, do not code here.

Necropsy Detection: This category refers to a situation in which the primary site of a lung cancer was first detected at necropsy. The detection could be a complete "surprise" (in which case a 0 is also entered in column 9); or an "identification", in which disseminated cancer was demonstrated or suspected during life, although a primary site was never established.

(62): NECROPSY FINDINGS

A necropsy is considered "unrestricted" if it includes the thorax and abdomen, regardless of whether or not the head is examined. A "restricted" necropsy is confined to the thorax alone, abdomen alone, or head alone.

The following definitions are used for the terms cited in the coding:

"Tumor in thorax": Anywhere inside the chest, including chest wall and upper surface of diaphragm.

"Minimal amount of tumor elsewhere": Scattered deposits here and there; not enough in any single location per se to have been a major cause of death.

"Significant amount of tumor elsewhere": Strategic location (e.g., brain, both adrenals replaced) or quantity (e.g., massive replacement of liver) to have been a major contribution to the cause of death.

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- 0: Not applicable (no necropsy done or no data available)
- 1: No tumor present
- 2: Tumor present, confined to thorax
- 3: Tumor in thorax; minimal amount of tumor elsewhere
- 4: Tumor in thorax; significant amount of tumor elsewhere
- 5: No tumor in thorax; minimal amount of tumor elsewhere
- 6: No tumor in thorax; significant amount of tumor elsewhere
- 7: Necropsy restricted to thorax; tumor present
- 8: Necropsy restricted to thorax; no tumor found
- 9: Necropsy restricted to non-thoracic site (the findings are not coded)

(63) - (64): NECROPSY TISSUE

Use the Designation of Cell Types listed in Appendix D.

If several different types of tissue are mentioned at different locations, code the discrepancy in column 73. To choose which specimen to code here, use the following order of preferential topographic sites: primary parenchymal site; any endothoracic site; intra-abdominal sites; other.

(65) - (72): INTERVALS

A critical issue in determining these intervals is the selection of zero time, which is discussed in Appendix A. A problem arises when a patient has received thoracotomy as the second element of a pair or in a subsequent course of treatment. For the particular interests of our research in comparing the results of surgical therapy, we have taken the thoracotomy, whenever it occurred, as the date of zero time for coding the intervals in columns 65-72. This convention does not alter the chronological order in coding columns 47, 48 and 54.

The two chronometric intervals cited in these 8 columns should be recorded in months, with the decimal point placed as shown in the form. Do not enter another decimal point. A conversion table for changing weeks or days to months is contained in Appendix H. If there are two figures to the right of the decimal point, round off appropriately to one figure. (6.34 → 6.3; 6.25 → 6.3; 5.95 → 6.0; 5.85 → 5.9).

(65) - (68): PRE-TREATMENT INTERVAL (* TO ZT)

The selection of the "*" event is described in Appendix A.

When the interval can be exactly specified: code directly

Examples:

Value for * to ZT

Code As:

27.3

0	2	7	.	3
---	---	---	---	---

107.35

1	0	7	.	4
---	---	---	---	---

98.85

0	9	8	.	9
---	---	---	---	---

If the interval is more than 199.9, code as 199.9.

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When the interval cannot be specified exactly, use the following conventions:

Maximums (<): For a single interval code a 2 in column 65, and the value in columns 66-68. For example:

<3.6 mos. is coded as

2	0	3
---	---	---

 .

6

If the maximum interval is longer than 99.9 months, code as 299.9. If more than one interval is possible, use the convention below for coding uncertain intervals.

Minimums (>): For a single interval, code a "3" in column 65, and the value in columns 66-68. For example:

>12.3 mos. is coded as

3	1	2
---	---	---

 .

3

If the minimum interval is at least 99.9 months, code as 399.9.

Uncertains: If the interval is uncertain (i.e., two or more values are distinctly possible), code the largest value up to 99.9 months in columns 65-68. If larger than 99.9, code as 99.9. Note that a "metastatic" symptom of questionable attribution (coded in column 22) is eligible for coding in this column only if it is the shorter of two candidate intervals. Then use the following code for column 65:

<u>Value of Smallest Interval</u>	<u>Code Column 65 As:</u>
0 - <3 mos.	4
3 - <6 mos.	5
6 - <9 mos.	6
9 - <12 mos.	7
12 - <the other value in mos.	8

Examples:

<u>Value of * to ZT</u>	<u>Code As:</u>					
40.6 or 2.4 mos.	<table><tr><td>4</td><td>4</td><td>0</td><td>.</td><td>6</td></tr></table>	4	4	0	.	6
4	4	0	.	6		
240.6 or 12.6 or 5.7 mos.	<table><tr><td>5</td><td>9</td><td>9</td><td>.</td><td>9</td></tr></table>	5	9	9	.	9
5	9	9	.	9		
5.8 or 1.2 mos.	<table><tr><td>4</td><td>0</td><td>5</td><td>.</td><td>8</td></tr></table>	4	0	5	.	8
4	0	5	.	8		
14.5 or 7.67 mos.	<table><tr><td>6</td><td>1</td><td>4</td><td>.</td><td>5</td></tr></table>	6	1	4	.	5
6	1	4	.	5		
58 or 11 mos.	<table><tr><td>7</td><td>5</td><td>8</td><td>.</td><td>0</td></tr></table>	7	5	8	.	0
7	5	8	.	0		
24 mos. or 48 mos.	<table><tr><td>8</td><td>4</td><td>8</td><td>.</td><td>0</td></tr></table>	8	4	8	.	0
8	4	8	.	0		

None: If patient had no "* to ZT" interval, as will be the case for those with a 5 or 6 in column 9, code the duration of the "+ to ZT" interval. (The "+ to ZT" interval is described in Arch. Intern. Med. 123: 571-590 (May), 1969.)

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Unknowns: If the interval is unknown, code as 999.9. (This situation will occur occasionally in patients diagnosed during life, and is the usual circumstance for the "necropsy discovery" group.)

(69) - (72): POST-TREATMENT INTERVAL (ZT to END)

Column 69 is used for two purposes: (a) to indicate whether a patient is alive, dead, or of unknown status; and (b) to indicate the time interval elapsed between first anti-neoplastic therapy and primary surgery (zero time) in the cases in which another form of therapy precedes primary surgery. By further convention, categories 3-9 in the column take precedence over the entries 0-2. Categories 0, 1, or 2 may be used only in situations where primary surgery was not done, or was done without a preceding course of anti-neoplastic treatment.

- 0: Patient is dead and his survival data are known
- 1: Patient is a five-year survivor and still alive as of our last survey time
- 2: We do not know the current state of a patient for whom the known post-zero interval of life is less than five years. Code the known interval in columns 70-72
- 3: The interval between the beginning of the first anti-neoplastic treatment and primary surgery is ≤ 1 month
- 4: The interval is > 1 month but < 2 months
- 5: The interval is > 2 months but < 3 months
- 6: The interval is > 3 months but < 6 months
- 7: The interval is > 6 months but < 9 months
- 8: The interval is > 9 months but ≤ 12 months
- 9: The interval is > 12 months

Columns 70-72 are used to record survival in months from zero time. If survival time was longer than 99.9 months, record as 99.9.

(73): SPECIAL COMMENTS

Special Note: This category is used for any special note, written on the extraction form during its clinical review, that comments on the various diagnostic, therapeutic, or other judgments encountered in the patient's course. A description of the diverse content of these notes is presented on pages 588-589 of Paper IV in "The Epidemiology of Cancer Therapy", Arch. Intern. Med. 123: 571-590 (May), 1969. Also included in this category are post-zero para-clinical evidence of metastasis (e.g., abnormal LFT's) and systemic effects of the cancer (e.g., hypercalcemia) in the absence of clinical evidence.

The next two categories include histologic inconsistencies based on locations (discrepancy) or time of reading (disparity). The criteria for determining an "inconsistency" are presented in Appendix D. Cytology readings or negative readings are not included among candidates for histologic disparities and discrepancies. If an "inconsistency" is present, code as follows:

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Histology Discrepancy: Code here whenever the histologic citation made in any histologic coding field is based on a choice between different, but isotemporal, readings that are inconsistent. For example, if pre-zero bronchial biopsy is read as epidermoid carcinoma, and pre-zero scalene node biopsy is read as adenocarcinoma, this disagreement constitutes a discrepancy for coding columns 34-35.

Histology Disparity: Code when (a) an inconsistency occurs among the histologic diagnoses made at different readings of the same specimen, or (b) the histologic readings cited in columns 34-35, 51-52, 58-59, or 63-64 are inconsistent. Situation (a) usually occurs when the tissue specimens or slides are re-read at the index hospital after the patient was transferred from a previous hospital where specimens were originally obtained and interpreted.

(74) - (75): CARD NUMBER

For all formats in this coding series, this number is 02.

(76): ADDITIONAL DATA

This column is used to denote additional data that could not be cited elsewhere in the single Hollerith card format described by these criteria.

1: Reversible Co-Morbid Weight Loss: Significant weight loss ($\geq 10\%$ or ≥ 20 lbs. if % cannot be calculated) that is attributable only to a reversible co-morbid condition. Criteria for such weight loss are described in column 24.

2: Additional Card: Further details for this patient are coded on an additional Hollerith card.

4: Pre-Zero Morphologic Evidence of Brain Involvement: Code this category if the ultrathoracic morphologic evidence cited in category 4 of column 33 refers to tumor involvement of brain.

(77) - (80): PATIENT NUMBER

This is a four-digit coding number, arbitrarily assigned in sequence to each new patient in the series.

APPENDIX

- Appendix A: Chronometric Decisions
- Appendix B: Topographic Classifications
- Appendix C: Clinical Grouping
- Appendix D: Microscopic Classifications
- Appendix E: Examples of Coding of Radiographic Data
- Appendix F: Anatomic Grouping
- Appendix G: Therapeutic Classifications
- Appendix H: Chronometric Conversion Tables
- Appendix J: Diagnostic Classifications

APPENDIX A: CHRONOMETRIC DECISIONS

This coding system requires two critical decisions about chronometry in a patient's clinical course.

1. Selection of Zero Time

The first chronometric decision is the selection of a temporal reference point for the events of a patient's clinical course. This datemark, which we call zero time, allows the course to be divided chronologically into a pre-zero interval, zero time, and post-zero interval. The patient's condition at zero time then becomes the reference state at which diverse patients can be mutually compared.

The choice of this temporal reference point will vary with the purpose of the coding system. If an investigation is concerned mainly with the effects of treatment on "natural history", the best choice of zero time would be the date of first anti-neoplastic therapy, since this date would represent the first attempt to intervene in the patient's natural course. In ordinary clinical circumstances, however, a type of zero time occurs whenever a clinician makes a decision about anti-neoplastic treatment for a patient with cancer. At such times, the clinician would like to know the state and outcome of patients whose previous course had been comparable to that of the new patient. Since the new patient may or may not have received antecedent therapy, the appropriate comparative groups might not be found in data that have been coded according to a zero time and zero state based on the first therapy.

If warranted by the data and the purposes of the coding system, arrangements could be made to code the full details of each patient's condition at the time of each anti-neoplastic treatment. Such arrangements were not made here. The available data, although generally thorough for the patient's condition at the time of surgery or other types of first treatment, were not always equally detailed for the circumstances of subsequent therapy. Moreover, our investigation was concerned mainly with the way "natural history" had been affected by surgery in operable patients or by other therapeutic agents in patients regarded as inoperable. Accordingly, the following conventions were developed for the selection of zero time:

If the primary site of the cancer is surgically explored, with a pre-operative goal other than biopsy alone, the date of that surgery is zero time, regardless of whether the cancer was removed, and regardless of whether the patient had received previous anti-neoplastic therapy. If there was no primary surgery, zero time is the date of whatever anti-neoplastic treatment was given first. If "metastatic surgery" -- such procedures as craniotomy, laparotomy or laminectomy -- was performed before other modes of anti-neoplastic treatment, and if a significant amount of neoplastic tissue was removed, the metastatic surgery is regarded as zero time treatment. The amount of removed metastatic tumor is regarded as significant if reported in such phrases as "tumor enucleated" or "a large portion of tumor was excised". Alternatively the amount will be regarded as significant if the quantity of removed tissue cannot be determined from the record, and if there is no statement that the excised specimen was a biopsy. If the amount of removed tissue is not significant by these criteria, the metastatic surgery is regarded as a pre-biopsy, and the choice of zero time depends on subsequent anti-neoplastic therapy or therapeutic decisions. If no anti-neoplastic treatment was given, zero time is the date of the M.D.'s decision to give no treatment, or the date of the patient's refusal of offered treatment. If no therapeutic decision was made, zero time is the date of acquisition of the most recent diagnostic evidence that could have been followed by a therapeutic decision.

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The review of such diagnostic evidence should concentrate on its role in therapeutic decisions. Thus, the date of a metastatic series or a scalene node biopsy, performed for pre-therapeutic appraisal of the cancer's extensiveness, would be a more cogent selection than the date of a repeated chest X-ray, performed to follow the progress of a pneumonia.

An exception to these principles occurs in situations where the patient remained untreated for a long time after a decision not to give anti-neoplastic treatment while the patient was in a relatively favorable stage of the cancer. This contra-therapy decision may have been made by an M.D. or by the patient, who refused an offer of thoracotomy, primary radiotherapy, or pre-therapeutic "work-up". Thereafter, the patient remained untreated until the development of new events, leading to an advanced or pre-terminal stage of the cancer, when usually the patient receives chemotherapy or metastatic therapy. In such circumstances, the initial decision against treatment can be regarded as zero time; and the later anti-neoplastic treatment can be coded as "subsequent" therapy. The definition of an "advanced" or "pre-terminal" stage will vary with different situations, as will the definition of the "long time" in which the patient remained untreated. In general, the development of metastatic or of major "systemic" phenomena that did not exist previously can be regarded as "advanced", and an untreated interval of 6 months or more can be regarded as a "long time". When alternative criteria are used for these decisions, an appropriate entry should be made in the running log, so that consistency can be maintained in later decisions for comparable cases.

A detailed discussion of zero time appears in Arch. Intern. Med. 123: 323-344 (March), 1969. A flow chart for the decisions, omitting the exception noted in the preceding paragraph, is presented on page A-4.

2. Selection of Zero State

The coding of columns 3-46 depends on the patient's zero state, which represents his condition at zero time, and includes data of the clinical and para-clinical events that occurred during the "present illness", as well as data about the diagnostic and prognostic co-morbidity present at zero time. The "present illness" begins with the inception event, described in section 3.

In consolidating the available data for coding, the following conventions are used:

a. "Greatest Extent" Convention

For endoscopic and microscopic evidence (bronchoscopies, biopsies, and cytologies), code the greatest extent of positive findings noted during the present illness. Thus, if a mass was seen at one bronchoscopy but not seen at a later bronchoscopy, code the existence of a visible mass (unless there is reason to believe that the first bronchoscopy is unreliable). Similarly, if the cytology of a pleural effusion is positive at a first thoracentesis but negative later, code the positive finding.

b. "Most Recent" Convention

For radiographic evidence, code the results that were closest to zero time in commensurate examinations of the same region. Thus, if routine Chest X-ray showed

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"hilar involvement" that later disappeared (on routine Chest X-ray), do not code the hilar involvement. If the hilar involvement was noted on routine Chest X-ray but not noted at laminography (or vice versa) the hilar involvement should be coded. If the "disappearance" or "appearance" of a manifestation represents a disagreement in radiographic interpretations of films on a single date, rather than a change in films for two dates, code either the "greatest extent" of noted lesions, or the opinion of the radiologist selected for preferential consideration, or the ambiguity.

This same convention applies to certain other types of data. For multiple values of weight, pre-transfusion hemoglobin or hematocrit, and para-clinical laboratory tests, code the values closest to, but before, zero time.

c. "Symptom Disappearance" Convention

Symptoms that appeared during the present illness, and that are attributable or possibly attributable to the cancer, need not persist to zero time to be coded. Primary symptoms that have entirely disappeared before zero time can be recorded appropriately for their existence, regardless of whether they disappeared spontaneously or after treatment. The disappearance of such manifestations can be cited appropriately (if no systemic or metastatic symptoms can be coded) under "Transient Primary Symptoms". In patients whose zero time is at a thoracotomy that was preceded by anti-neoplastic therapy, antecedent systemic or metastatic symptoms can be coded, although absent at zero time, if their amelioration can be explained by the earlier therapy. Thus, HPO-type joint pain disappearing after radiotherapy or focal CNS symptoms alleviated after craniotomy, can be coded as part of the total events that had occurred during the present illness that is "summed" in the account of zero state.

d. Precedence of Conventions

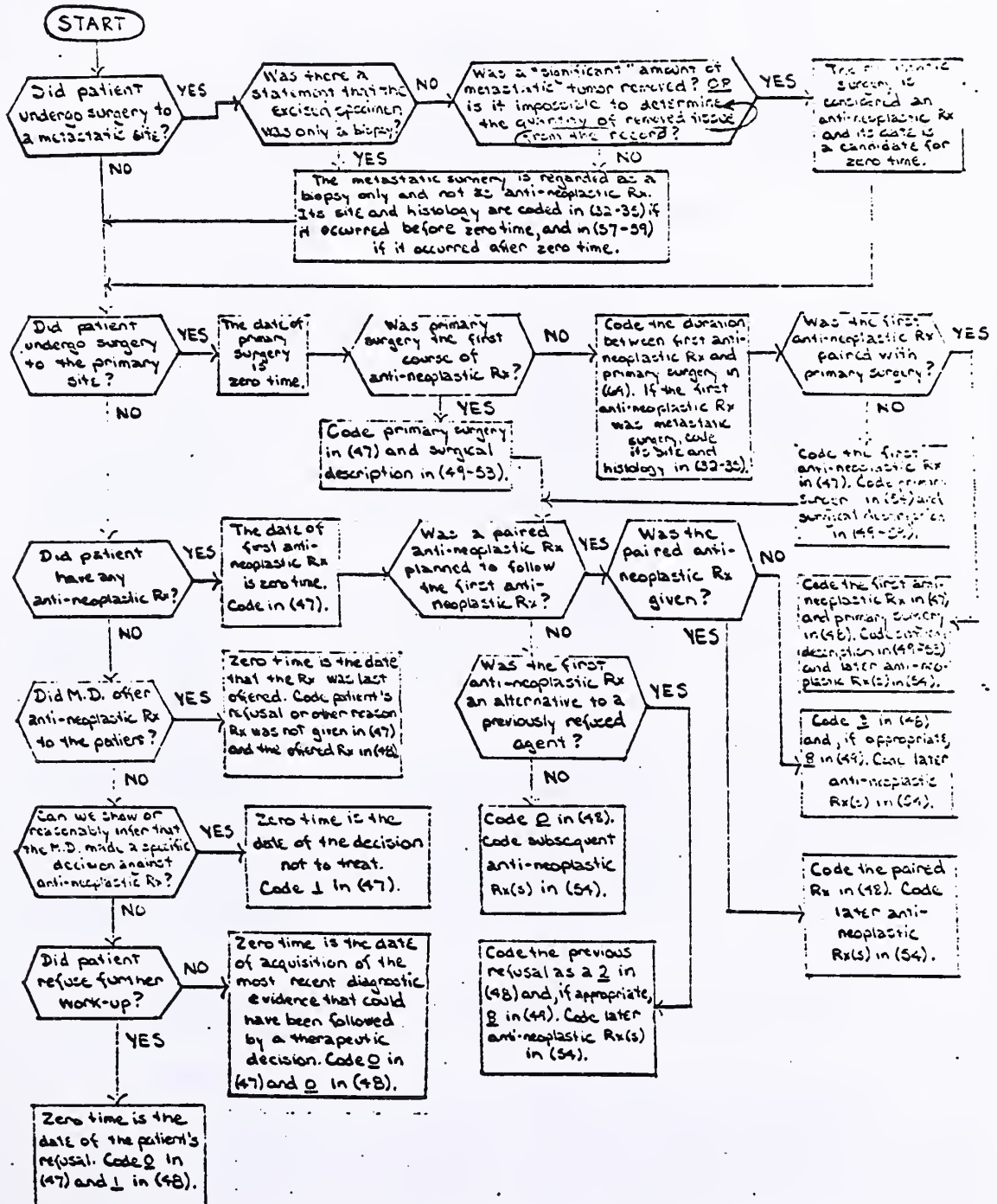
If evidence of tumor involvement of a particular anatomic site is obtained from both radiographic and surgical procedures, then the "greatest extent" convention, takes precedence over the "most recent" convention for coding both types of data. For example, if a cranial metastasis demonstrated on X-ray by pineal shift is removed at pre-zero craniotomy and a subsequent pre-zero skull film is read as normal for pineal shift, the initial, positive X-ray finding should be coded, as well as the positive microscopic evidence obtained at craniotomy.

3. Selection of the Inception Event

The second main chronometric decision is the selection of the inception event, which is the earliest symptom or clinical event (such as pneumonia) that is diagnostically attributable or questionably attributable to the lung cancer. Metastatic symptoms of questionable attribution can only compete in the coding for the inception event if they are of a shorter duration than the other possible candidates. [A discussion of the attribution decisions appears in Arch. Intern. Med. 123: 448-461 (April), 1969 and in J. Chron. Dis. 23: 455-469 (Dec.), 1970.] The inception event, also known as the asterisk event ("*" event), thus denotes the onset of the "present illness" for the lung cancer. The choice of this event is further discussed in Arch. Intern. Med. 123: 448-461 (April), 1969 and Arch. Intern. Med. 123: 571-590 (May), 1969.

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Flow Chart for Coding First Therapeutic Action
and Zero-time Events



APPENDIX B: TOPOGRAPHIC CLASSIFICATIONS

The nomenclature developed here is needed for several types of coding in which the location of a structure must be classified. The classifications occur during the coding of metastatic symptoms in columns 19-21; during Anatomic Grouping (see Appendix F); during the coding of radiographic data in columns 36-42; and during the coding of columns 31, 32, 33, and 55-57.

Three different concepts are involved in these classifications: contiguity, lateralization, and location.

1. Categories of Contiguity

Two lesions at two discretely different locations are said to be contiguous if they have a direct anatomic connection between them. For example, if a tumor grows outward from bone toward the surface, invading muscle and skin, each of these three separate locations -- bone, muscle, and skin -- will contain tumor, but the tumor in muscle is contiguous to bone; and the tumor in skin is contiguous to muscle. Similarly, when a tumor of the lower part of the upper lobe of a lung grows across the fissure lines into the upper part of the lower lobe, the two locations -- upper lobe and lower lobe -- are involved contiguously. On the other hand, if the upper part of the upper lobe and lower part of the lower lobe are each involved separately, without any direct anatomic "bridge", the lesions at these two locations are non-contiguous.

The importance of contiguity is its role in indicating how far a tumor has spread from the site of origin. Thus, in the two examples just cited of upper and lower lobe involvement, the tumor has spread more widely in the second case than in the first, even though the same lobes are involved in both instances. As another example, consider a patient who has lung cancer in a rib; a primary tumor near the hilum has spread farther to reach the rib than a peripherally located primary tumor that has invaded the rib contiguously.

The contiguity of anatomic involvement can readily be determined when data are available from surgery or from necropsy. Such data are not available, however (or cannot be used) for the classifications performed at zero time and at many other "datemarks" of classification. In such circumstances, decisions about contiguity will depend on clinical evidence obtained by inspection and palpation, and on para-clinical evidence obtained from radiography, endoscopy, and microscopic examinations. Two lesions will be called contiguous if the available evidence suggests that they are anatomically connected. If the evidence of a direct connection is dubious, unavailable, or negative -- and if a positive inference cannot be made -- the two lesions will be called non-contiguous.

In lung cancer, the questions of contiguity will usually arise for lesions within the lung and in peripulmonic tissues that are adjacent to the lungs (mediastinal structures, pleura, bones, chest wall, skin).

a. Intrapulmonary Contiguity

If two different lobes, segments, or discrete parts of the same lung are involved by tumor, they may be regarded as contiguous unless the X-ray report specifically indicates that they are not. For example, such citations as "one lesion is metastatic from the other" or "diffuse nodules" would indicate non-contiguity; or, if one lesion is clearly at the apex of the lung, any other lesion in a distal site of

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the parenchyma will be non-contiguous.

b. Peripulmonary Contiguity

A tumor that is centrally located, in or near the hilum can spread contiguously to the "inner thoracic region" of hilar nodes and mediastinal structures. A tumor that is peripherally located -- at the apex or near the parietal pleura -- can spread contiguously to the "outer thoracic region" of the pleura and structures of the thoracic wall and skin.

The following conventions are used for coding "inner" and "outer" contiguity.

1). Inner Contiguity

At zero time, involvement of hilar and mediastinal nodes is regarded as contiguous. At subsequent "datemarks", this involvement may be marked as non-contiguous if direct anatomic evidence from surgery or necropsy has demonstrated the presence of a peripheral primary tumor.

At zero time, involvement of "mediastinal viscera" (as defined later in this appendix) is regarded as non-contiguous. At subsequent "datemarks", this involvement may be marked as contiguous if direct anatomic evidence has demonstrated that the source of the primary cancer is adjacent to the involved "viscus" or "viscera".

2). Outer Contiguity

An "outer" lesion may be considered contiguous if at least one of the three following criteria has been fulfilled:

a). The primary site of the tumor, as demonstrated on X-ray, is peripheral (or apical); and the involved site (in bone, chest wall, or skin) is adjacent to the primary, as demonstrated by roentgenography and/or clinical examination. For example, X-ray may show the primary tumor near the chest wall, and palpation may show a hard mass in the adjacent chest wall.

b). The presumptive primary site of the tumor and the "outer" structure are involved together in a lesion whose topographic components cannot be distinguished. For example, an infiltrate in the apex may destroy part of a rib, without clear definition of which part of the total lesion is the "primary".

c). A lesion develops in an "outer" structure that is the site of previous surgery. For example, tumor nodules may develop along the line of a thoracotomy scar, or in the track of a needle biopsy.

2. Categories of Laterality

The term "laterality" is used for at least two different purposes in labelling thoracic structures: to denote the site of a single structure as being "central" or "lateral"; and to denote the relationship of a given structure to the primary as either ipsilateral or contralateral.

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a. Single Sites

A structure is lateralized if it can be labelled as being on either the right or left side of the chest. The following structures are lateralized: bronchi, pulmonary parenchyma, hilum, pleura, recurrent laryngeal nerve, ribs, chest wall, scapula, clavicle, diaphragm. The following structures are central (or non-lateralized): sternum, thoracic vertebrae, intrathoracic spinal cord, mediastinal nodes, and all mediastinal "viscera" except the diaphragm and the recurrent laryngeal nerve. A central structure is sometimes cited in a way that lateralizes it; thus, a radiologist may describe nodes in the "right mediastinum".

b. Inter-Relationship to Primary Site of Tumor

Any structure in the chest can be classified as ipsilateral ("same side") or contralateral ("other side") in its relationship to the side of the primary tumor. As an arbitrary convention, any central structure will be regarded as ipsilateral, and so the question of classification arises only for lateralized structures in relation to a lateralized primary.

The primary tumor is lateralized if its site of origin can be located on one side of the chest. Occasionally, the primary tumor cannot be lateralized, as in these examples: no primary site identified on the chest X-ray; primary site appears to be in central mediastinum; chest shows bilateral neoplastic involvement, with no primary side discernible. If no primary site has been identified, the side of an isolated unilateral abnormality believed due to the cancer may be regarded as the side of the primary. For example, the right pulmonary parenchyma may be obscured by a neoplastic pleural effusion, while the left lung is clear; in this circumstance, the tumor may be regarded as lateralized on the right side.

3. Categories of Location

The use of these categories in the staging of Anatomic Groups (see Appendix F) will depend on features of laterality and of contiguity.

a. Endothoracic Structures

- 1). Endopulmonic: bronchi and pulmonary parenchyma
- 2). Peripulmonic:
 - a). Outer zone: visceral or parietal pleura; chest wall (muscles, nerves, or "chest wall" without other specifications); endothoracic bones (ribs, thoracic vertebrae, sternum, xiphoid, manubrium), intrathoracic spinal cord.
 - b). Inner zone (mediastinum):
 - (1). Lymph nodes (hilar, mediastinal, carinal, paratracheal, peri-aortic).
 - (2). Mediastinal "viscera" (trachea, esophagus, heart, major vessels [aorta, pulmonary artery, pulmonary vein, superior vena cava, inferior vena cava], recurrent laryngeal nerve, diaphragm, phrenic nerve. The carina is not considered to be a mediastinal viscus).

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b. Perithoracic Structures

- 1). Parathoracic lymph nodes (scalene, supraclavicular, and/or axillary).
- 2). Parathoracic bones (scapula, clavicle).
- 3). Skin and subcutaneous tissues covering the thorax.

c. Ultrathoracic

Any structure beyond those cited in Sections a and b. This category includes:

- 1). Cervical and other non-parathoracic lymph nodes; skin and subcutaneous structures.
- 2). Non-thoracic vertebrae and other bones.
- 3). Brain and skull.
- 4). Abdominal structures: liver, pancreas, etc.

APPENDIX C: CLINICAL GROUPING

The codes here represent an arbitrary system developed during this research to classify "suspicious" symptoms that are either definitely or questionably attributed to the lung cancer. These categories are used for coding column 23.

- 1: "Asymptomatic": No "suspicious" symptoms.
- 2: "Long Pulmonic": The patient must have none of the symptoms of groups 3 and 5 below, and one or more of the following "suspicious" symptoms: recent new cough or change in pattern of chronic cough; hemoptysis; subjectively noted wheeze; recent dyspnea; thoracic ache or pain; or a clinical manifestation of pulmonary infection. At least one of these symptoms must have been present for 6 months or more. By convention, appropriately symptomatic patients with an ambiguous duration for the * to ZT interval (i.e., one reported value is less than 6 months, and another reported value is at least 6 months) or patients whose duration is uncertain (i.e., columns 65-68 are coded as 999.9) are also classified as "Long Pulmonic".
- 3: "Short Pulmonic": The same types of symptoms cited in group 2 above, except that all of the symptoms must have a pre-zero interval of less than 6 months. No symptoms of groups 4 and 5 below.
- 4: "Systemic": The patient must have at least one of the symptoms cited in this category, and none of the symptoms of group 5. Symptoms of groups 2 and/or 3 may or may not be present. The appropriate symptoms for group 4 are: persistent anorexia, weight loss as a presenting complaint; persistence of weakness, fatigue, or significant malaise; clubbing noted by the patient; significant clubbing noted by M.D.; joint pain due to HPO (hypertrophic pulmonary osteoarthropathy); or a special paraneoplastic syndrome due to "hormonal" secretion by the lung cancer. Among the syndromes included in this last category are: inappropriate secretion of vasopressin (ADH); neuromyopathy that has been specifically diagnosed as due to "hormonal" rather than anatomic metastatic causes; Cushing's syndrome; and carcinoid syndrome. The systemic symptoms are represented by any positive entry in columns 17 or 18, or categories 4, 6, or 8 in column 16. By convention, objective evidence of substantial weight loss, although not strictly a "symptom", is also included in this clinical group. The appropriate categories are 1, 2, 3, or 4 in column 24.
- 5: "Metastatic": The patient must have at least one of the entities cited as a mediastinal, regional, or distant metastatic symptom definitely attributable to the spread of the cancer. Symptoms from groups 2, 3, and 4 may or may not be present.

APPENDIX D: MICROSCOPIC CLASSIFICATIONS

This appendix provides (1) a coding taxonomy for designating cellular types, (2) instructions for making a choice among competing specimens, and (3) a classification of histologic inconsistencies. For the microscopic designations on this page, the negative code is used if a biopsy specimen is reported as "suggestive of cancer", without specification of a cellular type.

1. Designation of Cell Types

- 00: Not applicable (not done, unsatisfactory, or none available)
- 01: Negative biopsy
- 02: Negative pap smear or negative cell block
- 03: Negative onkosponge
- 04: Positive pap smear (other than sputum)
- 05: Positive cell block
- 06: Positive onkosponge
- 07: Positive sputum cytology

- 10: Epidermoid (Squamous-cell) Carcinoma [Use this Dx if the Ep. CA is not further specified]; (WHO 1)
 - 11: Highly differentiated Ep. CA; Well diff. Ep. CA; (WHO 1a)
 - 12: Moderately differentiated Ep. CA; Diff. Ep. CA; (WHO 1b)
 - 13: Slightly diff. Ep. CA; Poorly diff. Ep. CA; Mod. Undiff. Ep. CA; (WHO 1c)
 - 14: Anaplastic Ep. CA; Pleomorphic Ep. CA; Polymorphous Ep. CA
 - 15: Undifferentiated Ep. CA; Dediff. Ep. CA; Undiff. epithelial CA
 - 17: Carcinoma in situ

- 20: Small-cell CA (Undifferentiated Small-cell CA); (WHO 2)
 - 21: Oat cell CA; Oval-cell structure; (WHO 2a)
 - 22: Polygonal cell structure; (WHO 2b)

- 30: Adenocarcinoma; Well differentiated Adenocarcinoma; Mucinous Adeno. CA; (WHO 3)
 - 31: Acinar; (WHO 3a)
 - 32: Bronchiolar CA; Papillary (alveolar cell); Papillary (mucous-producing) Adeno CA; (WHO 3b)
 - 33: Chiefly large cells; (WHO 3c)
 - 34: Anaplastic Adenocarcinoma
 - 35: Undifferentiated Adenocarcinoma; Poorly differentiated Adeno CA

- 40: Large-cell undifferentiated carcinoma; (WHO 4)
 - 41: Giant-cell anaplastic
 - 42: Pleomorphic
 - 43: Plexiform

- 50: Combined Epidermoid and Adenocarcinoma; (WHO 5)
- 51: Combined Small-Cell and Adenocarcinoma
- 55: Anaplastic Carcinoma; Poorly diff. CA; Undiff. CA; Anaplastic scirrhus CA
- 56: Bronchogenic Carcinoma
- 57: Carcinoma [Type unspecified]; Malignant tumor cells [Type unspecified]

- 60: Bronchial Adenoma [Type unspecified]
 - 61: Carcinoid Type
 - 62: Cylindroid Type

- 70: Mesodermal Tumor [Type unspecified] (sarcoma)
 - 71: Fibroma
 - 72: Fibrosarcoma

- 76: Cancer other than CA lung (includes malig. melanoma)
- 77: Metastatic Cancer
- 80: Cancer grossly visualized at time of exploratory surgery
- 81: Cancer grossly visualized at endoscopy [Description must say "cancer" or "neoplasm", not just "mass"]

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In the list of codes on the preceding page, the numbers and letters in parentheses after the letters WHO represent the coding citations used in the original World Health Organization classification, as reported by Yesner, R., Gerstl, B., and Auerbach, O. in Ann. Thorac. Surg. 1: 33-49 (January), 1965.

2. Choice of Competing Specimens

The coding system contains four "datemarks" for recording microscopic evidence of cancer: columns 34-35, 51-52, 58-59, and 63-64. If several types of evidence, or evidence from several sites, are available as competitors for citation at a particular "datemark", a decision must be made about which evidence to code for that "datemark".

If several types of evidence are available, use the following order of preference: positive histology (codes 10-57, 70; 72-77); positive cytology (codes 04-07); positive gross visualization (codes 80, 81). The exception to this preferential order occurs when a thoracotomy patient has a negative pathology report. Since the information regarding gross visualization of tumor will already be coded in column 53, code the negative pathology finding in columns 51-52.

If histologic evidence is available from several sites, a specimen from lung or bronchus is preferred. Use the following order of preference: lung biopsy; bronchoscopy; parathoracic node; other. If more than one positive cytologic specimen exists; choose in the order of 04 first, descending to 07. If more than one gross visualization exists, choose the one at which an endopulmonic or endothoracic site was inspected. If all specimens are negative, code in the order of preference descending from 01 to 03. If no evidence is available, code 00.

3. Classification of Histologic Inconsistencies

A histologic inconsistency exists when two histologic readings for the same cancer are not exactly the same. If the readings compete for coding in the same "datemark" position, the disagreement is called a discrepancy. If the same slide has received several readings that do not agree, or if the histologic specimens at several datemarks do not agree, the situation is called a disparity.

Despite the issues of location and timing that distinguish discrepancies from disparities, an "inconsistency" in two readings must also be defined. The "disagreement scale" listed here is derived from the investigation reported in Am. Rev. Resp. Dis. 101: 671-684, 1970. In this list, each pair of hyphenated numbers represents the two available histologic readings.

In the sections that follow three different grades of disagreement are cited. The non-italicized pairs of numbers were assigned to one of the three grades of disagreement during the cited investigation. The italicized pairs were added by extrapolation from that study's basic principles to cover additional disagreements encountered in the present investigation.

Grade 1: Slight Disagreements

10-17; 11-12; 13-40; 13-55; 14-55; 15-55; 20-21; 20-22; 20-57; 21-22; 21-55;
21-57; 22-55; 30-31; 30-32; 30-33; 31-32; 35-40; 40-42

Grade 2: Definite Disagreements

10-11; 10-12; 10-13; 10-15; 10-42; 10-50; 10-55; 11-13; 11-14; 11-55; 12-13;
12-55; 13-20; 13-22; 13-33; 13-34; 13-35; 20-35; 20-55; 21-32; 21-55; 22-40;
30-35; 30-50; 30-55; 31-33; 32-33; 32-35; 32-55; 32-60; 33-40; 33-50; 34-55;
35-55; 40-55; 40-56; 40-60; 42-55; 50-55

Grade 3: Major Disagreements

10-30; 10-31; 10-32; 10-33; 10-40; 10-60; 11-21; 11-31; 11-40; 11-60; 12-21;
12-22; 12-30; 12-32; 12-33; 12-40; 12-60; 13-21; 13-30; 13-31; 13-32; 13-50;
13-60; 20-40; 21-31; 21-40; 30-40; 31-40; 32-40; 40-50

For practical purposes, differences that are only "slight disagreements" will not be coded as "inconsistencies", and this term will be restricted to "definite" and "major" disagreements. If a particular pair of discordant readings is not cited in the above list, an ad hoc decision is required about the magnitude of disagreement.

Classification of Histologic Type

	<u>Codes</u>
Well-differentiated Epidermoid Cancer	10,11,12,17
Well-differentiated Adenocarcinoma	30,31,32,50
Anaplastic	13,14,15,20,21,22,33,34,35,40,41, 42,43,55,57,51
Metastatic, not otherwise specified	77
Cytology only	04,05,06,07

Order of Precedence for Competing Specimens

- 1) Zero Time Thoracotomy
- 2) Pre-Zero Time Bronchoscopy or Lung Biopsy
- 3) Necropsy Tissue
- 4) Other Zero Time Tissue
- 5) Other Pre-Zero Time Biopsy
- 6) Post-Zero Time Biopsy

APPENDIX E: EXAMPLES OF CODING OF RADIOGRAPHIC DATA

The examples provided in this appendix are intended to illustrate the arbitrary conventions used for coding special situations in radiographic data.

1. Primary Site Unspecified

a. Only one side of the chest is involved, primary parenchymal site not discerned:

	(37)	Columns (38)	(40)	(41)
Lung obscured by massive opacity	<u>3</u> or <u>4</u>	<u>6</u>		
Lateralized pleural effusion; no other lesion evident	<u>3</u> or <u>4</u>	<u>5</u>		
Lateralized bony or chest wall lesion; no other distinct lesion visible	<u>1</u> or <u>2</u>	<u>0</u>	<u>6</u>	

b. Lung parenchyma is bilaterally involved:

No extraparenchymal lesions	<u>7</u>	<u>0</u>	<u>0</u>	<u>4</u>
Rib involved on one side	<u>7</u>	<u>0</u>	<u>4</u>	<u>4</u>
Ribs involved on both sides	<u>7</u>	<u>0</u>	<u>4</u>	<u>4</u>
Pleural effusion on one side	<u>7</u>	<u>0</u>	<u>1</u>	<u>4</u>

2. Atelectasis

"Atelectasis" is an interpretation given to an X-ray shadow. The interpretation generally implies the radiologist's belief that the shadow is not neoplastic, but a neoplasm may be interpreted fallaciously as merely atelectasis, because (1) the tumor may be small, but big enough to block a bronchus, creating atelectasis beyond the site of the block; or (2) this neoplastic shadow may be the only abnormal shadow in the parenchyma. If another and more clearly neoplastic shadow has been described by the radiologist, an "atelectatic" area, reported in the same reading, is probably not regarded as neoplastically involved.

Situations involving atelectasis are coded as follows: if the only evidence of involvement is an atelectatic lobe, code the lobe in columns 37-38. If hilar or mediastinal nodes are involved in addition to the atelectatic lobe, code the lobe in columns 37-38 and the nodes appropriately in columns 39 or 41. If the only evidence of contralateral involvement is an atelectatic lobe, code 1 in column 41 for "questionable involvement".

3. Main Bronchus

The radiographic coding of involvement of a main bronchus should be based on radiographic evidence alone. Endoscopic evidence, if present, is coded separately in column 29, and should not be used here. The radiographic coding for main bronchus is as follows: If only the right or left main bronchus is involved, code 3 or 4 in column 37, and 8 in column 38. If the right or left main bronchus is

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involved and a lobe is atelectatic, code only the main bronchus in columns 37-38.

If a lobe is specified as involved on gross films, but the main bronchus (and not the lobe) is specified in the reports of laminography, code only the involved lobe in columns 37-38. If the gross film specifies main bronchus and only the lobe is reported at laminography, code only the lobe in columns 37-38.

If an involved hilum is reported in gross films, but the main bronchus is reported in laminography, code 3 or 4 in column 37, 8 in column 38, and 1 in column 39.

APPENDIX F: ANATOMIC GROUPING

The classification of anatomic groups depends on the type of evidence and the topographic site and contiguity of the involvement. A discussion of topography and contiguity is contained in Appendix B.

A. TYPE OF EVIDENCE

Anatomic grouping requires evidence of structural lesions regarded as showing neoplastic involvement. A positive finding in any of the categories cited here will denote such involvement.

1. Microscopic: pap smear, cell block, onkosponge, aspiration biopsy, needle biopsy, operative biopsy.

2. Radiographic: a density, mass, infiltrate or other abnormal radiographic shadow strongly suspected as neoplastic, or related to neoplasm. A pineal shift on skull X-ray denotes intra-cranial tumor unless otherwise interpreted.

3. Gross Anatomic: tumor grossly visible at endoscopy or at surgical exploration regardless of whether or not tumor is excised or demonstrated microscopically. Since positive findings at bronchoscopy or tracheoscopy identify the primary site of the tumor, but not its extra-pulmonic anatomic extensiveness, such findings will never be used in these groups.

4. Clinical Examination: unequivocal visualization or palpation of tumor in superficially palpable masses (including lymph nodes); or in liver or other palpable organs.

5. Para-Clinical Examination: bloody, pink, or sero-sanguinous pleural fluid, in the absence of some other explanation for the blood. The blood must therefore be found in a "first tap" specimen, and should not be attributable to an isolated pneumonia, infarction, or other non-neoplastic lesion.

B. ANATOMIC GROUPS

Anatomic staging is intended to indicate the topographic extensiveness of tumor involvement beyond the endopulmonic tracheo-bronchial tree. Bronchoscopy, which reveals central location and resectable margination of the tumor, is not used to classify topographic extensiveness.

The anatomic groups are listed here in reverse order. These same numbers are used for coding in column 43. At any level of the grouping, a member of one of these groups must have none of the characteristics of the higher groups (except 6), but may have many characteristics of the lower groups.

6: "Unknown": Used for "necropsy surprise" cases.

- F2 -

5: "Ultrathoracic": Involvement of any structure cited topographically as ultrathoracic. The perithoracic skin and/or subcutaneous tissues are coded as ultrathoracic if they are not contiguously involved with an "outer-zone" peripulmonic or perithoracic structure.

4: "Contrathoracic": Contralateral involvement of any endothoracic, peripulmonic, or perithoracic structure. Includes cases in which tumor crosses the mediastinum to involve the hilum or other contralateral structures contiguously.

3: "Isothoracic": Ipsilateral involvement, without contiguity of any one of the following structures: another part of the same lung; any peripulmonic "outer-zone" structure; any mediastinal "viscus"; or any perithoracic structure. (Skin and subcutaneous tissues may be classified as isothoracic only if contiguously involved with chest wall. The chest wall would be classified as isothoracic only if not contiguously involved with underlying primary tumor.) Tracheal involvement on bronchoscopy is not considered isothoracic involvement for anatomic grouping.

2: "Vicinal": Lymph nodes of the hilum or mediastinum, or ipsilateral contiguous involvement of any peripulmonic structure.

Note: The perithoracic bones and lymph nodes are seldom contiguously attached to primary tumor; when they are, they may be coded in this category.

1: "Endopulmonic": None of the above. This category may also be coded, in the absence of any other topographic evidence, when the zero-state chest X-ray is read as "negative".

APPENDIX G: THERAPEUTIC CLASSIFICATIONS

1. Coding of Metastatic Surgery

If metastatic surgery was a therapeutic procedure (i.e., a significant amount of tumor was removed, as defined in Appendix A), its chronologic occurrence is coded appropriately as 9 in column 47 or 48, or as 4 in column 54. If it was part of the "first therapeutic action", its microscopy is recorded in columns 51-52, unless it was followed by thoracotomy. If followed by thoracotomy, metastatic surgery is still coded as 9 in column 47 or 48, but its site is recorded in column 32 or 33, and its microscopy in columns 34-35. The description of the thoracotomy is coded in columns 49-53, and its chronologic occurrence is coded, if a "paired" procedure, as 4 in column 48 or, if a "subsequent" procedure, as 1 in column 54. Column 69 is used to code the interval by which thoracotomy was preceded by metastatic surgery (or by any other first anti-neoplastic treatment coded in column 47).

If metastatic surgery was "subsequent treatment", its general site is coded in column 57, and its microscopy in columns 58-59.

2. Retrieval of Codes for Zero Time and First Therapeutic Decision

Because of the complexity of the codings for zero time and first therapy, the following outline is cited here for use in retrieval of therapeutic data during subsequent analyses. The contents of columns 47 and 48 are briefly summarized as follows:

Column 47

- 0: No decision
- 1: No Rx: M.D. decision
- 2: No Rx: Pt. refused
- 3: No Rx: Other reason
- 4: Thoracotomy
- 5: Primary Radiation
- 6: Cytotoxic
- 7: Primary Rad. + Cytotoxic
- 8: Rad. to Metastasis
- 9: Surg. or Focal Cytotoxic
to Metastasis

Column 48

- 0: No action
- 1: Pt. refusal of work-up
- 2: Alternate accepted
- 3: Planned paired Rx not given
- 4: Thoracotomy
- 5: Primary Radiation
- 6: Cytotoxic
- 7: Primary Rad. + Cytotoxic
- 8: Rad. to Metastasis
- 9: Surg. or Focal Cytotoxic
to Metastasis

a. The "Later Surgery" Group

According to the conventions described elsewhere (Appendix A, Section 1) surgery directed at the primary site is always regarded as zero time, no matter when it occurred in the therapeutic sequence. Consequently, patients who did not receive surgery as their very first treatment are first found via any of the codes 3-9 in Column 69. This "later surgery" subgroup can then be divided into two parts: the patients who had thoracotomy as the second element of a paired first treatment (4 in Column 48); and those who had thoracotomy as "subsequent treatment" (1, 3, 5 or 7 in Column 54).

The first therapeutic action for both these "later surgery" groups can be retrieved as described in the section that follows.

- G2 -

b. First Treatment

For all patients other than those just described in Section a, zero time and the first therapeutic action are identical. The codes for retrieval are as follows:

Patients with first treatment to primary site: 4 through 7 in column 47.

Patients with thoracotomy as first treatment: 4 in column 47.

Patients with first treatment to metastasis: 8 or 9 in column 47.

Patients with no treatment at zero time: 0 through 3 in column 47. (We can conclude that these patients never received anti-neoplastic therapy only if 0 is also coded in column 54.)

Patients with treatment planned but not given at zero time: 2 or 3 in column 47. The planned treatment is then found as 4 through 9 in column 48.

Patients who were offered, but did not receive thoracotomy: 8 in column 49.

APPENDIX J: DIAGNOSTIC CLASSIFICATIONS

During the retrieval and coding of the medical records, certain conventions were adopted for the diagnostic classifications in which each patient would be cited. The categories and methods of making these decisions are described in this Appendix.

1. Eligible Case: A patient who has satisfactory evidence to warrant the diagnosis of lung cancer. For certain types of analyses, microscopic evidence of cancer is a pre-requisite to diagnosis. For other analyses, the timing and hospital location of zero time are other pre-requisite conditions.

2. Apzer (Contraction of "Appropriate Zero") Cases: Eligible patients whose zero time occurred during a specified calendar interval at one of the index hospitals under survey. In this survey, the index hospitals are the West Haven VA Hospital and the Yale-New Haven Hospital. An otherwise eligible patient may be an "inapzer" case because zero time occurred at a different setting or outside the specified calendar interval, or both. The group of apzer patients form an inception cohort, as further defined in Clin. Pharm. Therap. 12: 864-879 (Sept.-Oct.), 1971.

3. Necropsy Specification Case: This type of patient, also called an "I-E" case in various places in this coder's manual, was known or suspected to have a cancer during life, but the exact source of the primary lesion was unknown or uncertain until demonstrated at necropsy. Necropsy specification cases are eligible for inclusion as apzers and many of the necropsy-specification cases were treated during life with an anti-neoplastic agent.

4. Necropsy Surprise Case: This type of patient, also called a "I-F" case in various places in this coder's manual, was found unexpectedly at necropsy to have a primary lung cancer that had not been diagnosed or seriously suspected during life. The pre-mortem clinical diagnosis may have contained no mention of a lung lesion; or a lesion, if noted, may have been attributed to inflammation, benign neoplasia, metastasis from an exopulmonic source, or some other disease that was definitely cited as something other than primary lung cancer. Anti-neoplastic therapy, if given, was begun with the diagnostic belief that the patient's disease was definitely not primary lung cancer. Although eligible for certain analyses, a necropsy-surprise patient cannot be an apzer case.

5. Para-Diagnostic Case: This diagnostic category is used for several different kinds of patients whose records were examined but not coded in the format described in this coder's manual.

a. Wrong Diagnosis: Lung cancer was initially diagnosed but later shown to be erroneous. The contradictory evidence may have been found at surgery, necropsy, or some other time in the clinical course. In the absence of surgery or necropsy, the contradictory evidence may have been total disappearance of the roentgenographic lesion(s) or other evidence suggesting false positive cytologic smears.

b. Equivocal Diagnosis: In the absence of surgery, necropsy, or contradictory evidence, the existing evidence of lung cancer was too equivocal for the patient's eligibility. There may have been uncertainty as to whether the pulmonary lesion was a carcinoma or uncertainty about whether a presumptive pulmonary carcinoma was primary in the lung or elsewhere.

- J2 -

c. Paramorphologic Case: This category consists of patients with diseases that may resemble lung cancer. Such cases can be divided into two groups.

1). Para-topographic: Cancer or benign tumor of the trachea, pleura or mediastinum.

2). Para-histologic: Benign or malignant lesions of ineligible histology. The malignant lesions include various sarcomas as well as Hodgkin's disease. The benign tumors include bronchial adenoma, hamartoma, mesothelioma, fibroma, neurofibroma, dermoid cyst, and teratoma. Other benign lesions are tuberculoma, granuloma, lipoid pneumonia, and "organizing pneumonia".

During this research, the records of patients with paramorphologic diagnoses were deliberately solicited and examined in order to find cases of lung cancer that may have received an erroneous citation in the SNDO or ICDA diagnostic codes used for the indexing of medical records. Such patients were also sought to obtain data about the epidemiologic spectrum of the "paramorphology" of lung cancer.

CRITERIA FOR CODING

Cancer of the Lung

Card No. 3: GENERAL SUMMATION

(1): Race

1= White

2= Black

3= Other

(2) - (9): TNM CLASSIFICATION¹

(2) - (9): Pre-Zero TNM Classification

Code in these columns the totality of anatomic evidence available at zero-time, prior to thoracotomy.

(2) - (3): Evidence for T3

Code any evidence that allows a classification of T3.

(2): Pleural Effusion

0 = None

1 = trace; e.g., "small amount of fluid in costophrenic sulcus"

2 = moderate; fluid was visualized at X-ray but does not qualify as category

1 or 3; or, uncomplicated thoracentesis yielded less than 1000 cc fluid;

or, chest was tapped only for diagnostic reasons. In the absence of

specification of the size of the effusion. Code the effusion as of

moderate size, by default.

¹The TNM (Tumor-Node-Metastasis) classification system employed here is a replica of that devised and used by the American Joint Committee (AJC). For a description of the TNM classification of malignant tumors of the lung, see the Amer. Joint Committee for Cancer Staging & End Results Reporting of Sept, 1973. Clinical Staging System for Carc. of the Lung.

These criteria for TNM classification were compiled by Dr. Feinstein and his clinimetric research group for the lung cancer cohort of 1953-1964

(2)[continued]

3 = massive; as coded on Card 02, where the effusion is of magnitude great enough to obscure the lung roentgenographically, or to create respiratory distress, or to evoke a therapeutic thoracentesis, or fluid volume that is cited as "large" or "moderately large". (Code here if on Card 02: Col. 40 = 1, 3, 5, or 7 and Col. 27 >0 and Col. 27 ≠ 8.)

(3): Other T3 Evidence

0 = None

1 = "Juxtacarinal"; tumor was shown bronchoscopically to be less than 2.0 cm distal to the carina; i.e., coded on Card 02 as Col. 29 = 1,2, or 3; which is a mass seen on bronchoscopy in or above the carina, or in the carina and at least one main bronchus, or in main bronchus close to the carina.

2 = Whole lung involvement; e.g., "lung obscured by massive opacity", "atelectasis of all three lobes" or primary tumor in main bronchus with total collapse of lung parenchyma distally.

Additive

4 = Adjacent structures; direct contiguous extension, as coded on Card 02, to one or more of the following: mediastinal viscera (category 4 in Col. 39 or any category in Col. 20), isothoracic structures on X-ray, other than multiple nodules (category 4 in Col. 40), microscopic proof of node (category 1 in Col. 32), pleura, pleural fluid, chest wall, or thoracic bone (category 2 in Col. 32), or palpable thoracic node (category 1 in Col. 31). If the involvement of these structures is non-contiguous,

(3)[continued]

- Additive {
- 4 = [continued] the lesion is regarded as metastatic and is coded as M1 in Col. 51, not here. Non-contiguous ipsilateral lesions in the lung parenchyma (multiple nodules) are coded only in Col. 49 as category 4. If information re: contiguity of other involvement is lacking, code adjacent structures here, and not metastatic involvement (Col.51): that is, assume contiguity when in doubt.
 - 8 = Non-specific; no statement of T3 evidence was made, but the tumor was judged to be of T3 extent. If coded here, a code of 8 may not be used in either Col. 47 or 48.

(4): Evidence for T2

Code evidence for assigning a classification of T2, regardless of existing evidence for T3 (Col. 45-46),

- Additive {
- 0 = None
 - 1 = Specific statement by radiologist of tumor size >3 cm.
 - 2 = Coder's assumption, from radiographic description, that tumor size is >3 cm. (e.g. described as a "mass", a "huge mass".) In the absence of a modifying phrase to indicate that a tumor is small enough for a citation in Col. 48, the tumor will be coded in Col. 47 as 2. A log will be kept of such codes to ensure consistency.
 - 4 = Spread to or toward the hilar region. This category refers to the extent of the primary, and does not include metastasis to hilar nodes (which are coded in Col. 50 as 1). An exception to this principle occurs when a hilar mass is described as present, without any further description. Such a circumstance is coded T2N1 (Col. 47 = 4, Col. 50 = 1). Some examples of phrases

(4)[continued]

Additive { indicating spread to or toward the hilar region are "supra-hilar", "parahilar", "tumor extends toward the hilum". When in doubt, the coder will refer the case to A.R.F. for decision, and record the case in the log, to ~~ensure~~ later coding consistency.

7 = mediastinal mass; no other evidence of primary tumor exists.

8 = Non-specific; no statement of T2 evidence was made, but the tumor was judged to be of T2 extent (e.g. atelectasis of less than the whole lung). If coded here, a code of 8 may not be used in either Col. 46 or 48.

NOTE: In the case of the 1^c tumor being located in the hilum or in the mediastinum, no assumption of size of the 1^c is coded here, as there is no way to distinguish between mass size caused by the 1^c tumor and that caused by nodal involvement.

(5): Evidence for T1

This column is used to code evidence for the T1 category, regardless of evidence for T3 (Col. 45-46) or T2 (Col. 47).

0 = None

Additive { 1 = Tumor stated to be ≤ 3 cm in greatest diameter (presumably surrounded by lung parenchyma)
2 = Tumor seen distally at bronchoscopy, Card 02, Col. 29 = 5,6; or tumor visualized at X-ray but bronchoscopic report refers to all bronchi being clear.
4 = Tumor visualized peripherally at X-ray or described as a "coin lesion".

(5)[continued]

8 = Non-specific; no statement of T1 evidence was made, but the tumor was judged to be of T1 extent, e.g. "parenchymal abnormality of an infiltrative type". If coded here, a code of 8 may not be used in either Col. 46 or 47.

(6): Pre-Zero T Classification of Primary Extent

Only one T class may be coded for each patient, as follows: If the tumor is classified as T3 (Col. 45 > 1 or Col. 46 > 0), Col. 49 = 3; if the tumor is classified as T2 in Col. 47, Col. 49 = 2; etc.

0 = Tumor proven only by bronchopulmonary secretions

1 = T1

2 = T2

3 = T3

4 = Multiple lesions in the same lung

7 = No evidence of 1° where clinical data (radiographic, bronchoscopic) are absent or inconclusive

8 = "TIS" (AJC); tumor in situ (must be described as such in the extraction form)

9 = No evidence of primary tumor, where clinical data form the basis of this conclusion

Coding Preference is given to the various T classifications as follows:

T3 > T2 > T1 > any other.

(7): Pre-Zero N Classification of Nodal Involvement

Only the highest N class is coded (if both hilar and mediastinal nodes are involved, code as 2). Most of the elements included here are already directly coded on Card 02.

0 = N0: no nodes seen on X-ray

1 = N1; X-ray visualization of ipsilateral hilum or hilar nodes (Card 02; Col. 39 = 1); or X-ray report of spread to "peribronchial nodes" at a distance from the hilum (such nodes are not coded on Card 02). Spread to nodes in the contralateral hilar region is not cited here. Such involvement is regarded as evidence of metastasis and is included in the M1 code (Col. 51) below.

2 = N2; X-ray visualization of mediastinal node involvement regardless of laterality (Card 02 category 2 in either column 39 or 41); or manifestations of mediastinal involvement which permit a clinical inference that mediastinal nodes are involved. (The candidates are the signs and symptoms listed for column 19 of Card 02. Hoarseness is regarded as sufficient evidence for coding N2 only if a) vocal cord paralysis was demonstrated on laryngoscopy, or b) this symptom was cited as a contra-indication for thoracotomy), or c) vocal cord not examined, but there was a substantial history of hoarseness (one month or more).)

(8): Pre-Zero M Classification of Metastasis

The elements included here are already directly coded on Card 02.

0 = M0; no evidence of metastasis

1 = M1; evidence of distant metastasis including ultrathoracic (Col. 42 > 0); or non-contiguous isothoracic other than multiple nodules (Col. 40 = 4,5), or regional nodes (category 1 in Col. 32), or pleura, chest wall or

(8)[1 = M1, continued]

thoracic bone (category 2 in Col. 32), or palpable thoracic, surface, or liver and other metastases (Col. 31); or pericardial effusion (category 1 in Col. 33); or contralateral pleural effusion (Col. 27 = 9 or Col. 41 = 1) or contralateral thoracic involvement (Col. 41 > 1) excluding mediastinal nodes (which are coded in Col. 50 as²); or non-contiguous thoracic symptoms (Col. 20); or symptoms of distant metastasis (Col. 21 > 0).

(9); Pre-Zero TNM Stage

The codes in Col. 49-51 are combined into a Pre-Zero TNM composite stage as follows:

- 1 = Stage 1; T1 NO MO, T1 N1 MO, T8 NO MO, T2 NO MO
- 2 = Stage 2; T2 N1 MO
- 3 = Stage 3; T3 with any N or M
 N2 with any T or M
 M1 with any T or N
- 9 = Unknown Stage; T0 NO MO
 T7 NO MO
 T9 NO MO
 T4 NO MO
 T4 N1 MO

(10) - (23): NEW DIAGNOSTIC TECHNIQUES

New diagnostic techniques refer to methods of diagnostic imaging available to define tumor extent in the 1977 cohort but not available to the 1953-64 cohort. In particular, these techniques were nuclear imaging, computerized tomography, and ultrasonic imaging.

For each test on the coding form, code the Result and Associated Clinical Evidence as follows:

(10), (12), (14), (16), (18), (20), (22): Result

- 0 = Negative result; This may be a reading of "negative", "within-normal-limits", or a similar reading denoting the absence of abnormal findings. A negative result may be coded if the study noted an abnormality which was clearly attributable to another disease, (examples: a bone scan positive in areas of known degenerative joint disease; a liver-spleen scan with abnormal uptake consistent with parenchymal disease in a patient with a history of cirrhosis)
- 1 = Positive result; Positive study showing an abnormality at a site other than the primary tumor, if the site of the primary is known
- 8 = Equivocal result; Refers to readings which are unable to clearly define an abnormality but are not felt to be normal. Readings may be "equivocal", or "possibly abnormal". This category may also be coded for instances when the official reading denotes a positive result without clear documentation of another reason for the abnormal study, but, the study is treated as if negative in the following work-up and therapy. Code 8 if the positivity of result is questionable.

X = Not done

(11), (13), (15), (17), (19), (21), (23): Associated Clinical Evidence

Associated clinical evidence refers to clinical or paraclinical data which might act as an impetus for performance of one of the new techniques, or which supports the result of the study when positive. The purpose of this category is to distinguish patients who were discovered to have more extensive disease as a result of screening as opposed to work-up of a specific complaint.

(11),(13),(15),(17),(19),(21),(23): Associated Clinical Evidence - cont.

0 = None; or, no study performed

1 = Yes; but questionably attributable to the cancer
(i.e. another potential cause of the evidence is present)

2 = Yes; clearly attributable to the cancer

8 = Yes; but evidence is of questionable existence

9 = UNK

(22) - (23): Other

When a study is performed which was not available in the 1953-64 study, and which is not listed on card 3, "other" will be coded if the study is performed to define tumor extent, and the type of study will be specified on the coding form.

(24) - (33): IMPACT OF NEW DIAGNOSTIC TECHNIQUES ON STAGING

Without Result of New Techniques: refers to the application of staging criteria with all pre-zero time information except that provided by the new techniques described in (10) - (23). If a positive result from a new study prompted the performance of a previously available study which was also positive, then the information provided by the "old" technique can be included in the staging for this category.

With Equivocal Results from New Techniques: refers to the application of staging criteria with all available pre-zero time information including results from new techniques which were positive and with results which were coded as equivocal now counted as positive.

(24) - (25): Toponymic Stage

(24): Toponymic stage without results of new diagnostic techniques;
coded as per (35)

(25): Toponymic stage with equivocal results from new techniques;
coded as per (35)

(26) - (33): TNM Stage

(26) - (29): TNM stage without results from new techniques;

(26): T ; coded as per (6)

(27): N ; coded as per (7)

(26) - (29): TNM stage without results from new techniques - cont.

(28): M ; coded as per (8)

(29): Stage ; coded as per (9)

(30) - (33): TNM stage with equivocal results from new techniques

(30): T ; coded as per (6)

(31): N ; coded as per (7)

(32): M ; coded as per (8)

(33): Stage ; coded as per (9)

(34): FUNCTIONAL SEVERITY

This is a composite stage of symptom severity and prognostic co-morbidity.
Code in descending order of precedence:

4 = IV = Severe prognostic co-morbidity

(code as per card 2 criteria for column 44 ; code here
if column 44 = 2,3,4,5,6, or 7)

and/or Severe tumor effects

(as per card 2 criteria for column 44 ; code here if
column 44 = 1,3,5, or 7)

and/or "Super Weight Loss"

(as per card 2 criteria for column 24 ; code here if
column 24 = 1, or 2)

3 = III = Quasimetastatic

(as per card 2 criteria for column 22 ; code here if
column 22 = 4,5,6, or 7)

2 = II = Severe dyspnea

(as per card 2 criteria for column 28 ; code here if
column 28 = 4,5,6, or 7)

and/or Recent dyspnea

(as per card 2 criteria for column 14 ; code here if
column 14 = 1,3,5, or 7)

and/or Systemic symptoms

(as per card 2 criteria for columns 16, 17, and 18 ;
code here if column 16 is greater than 4 ; and/or
column 17 or 18 are greater than zero)

(35): TOPONYMIC STAGE

This is a combination of morphologic and symptomatic evidence for tumor extensiveness. The composite contains 7 topographic strata. In descending order these are:

- 7 = Liver/Other - evidence of metastasis to deep, vital organs other than brain or bone, and beyond the thorax (see card 2 criteria for column 31, category 4)
- 6 = All Other Ultrathoracic Sites - evidence of metastasis to CNS, bone, surface nodules all beyond the thorax
- 5 = Intrathoracic - Implies massive spread within the thorax; includes massive pleural effusion, spread to contralateral lung or chest wall, or involvement of all three lobes on one side
- 4 = Isothoracic - non-contiguous spread within the thorax on the ipsilateral side.
- 3 = Vicinal - spread limited to contiguous sites; includes chest wall if a peripheral tumor, or hilar and mediastinal involvement if central. There must be no evidence of non-contiguity. (see card 2 coding criteria Appendix B for examples of contiguity)
- 2 = Symptomatic or Central - symptoms are bronchial, parietal, or parenchymal (other than dyspnea); central includes gross visualization near carina or involvement of 2 lobes on chest x-ray.
- 1 = Asymptomatic and Peripheral

(36): COMPOSITE STAGE

This is a combination of Functional Severity Stage and Toponymic Stage to form 5 strata as follows:

Toponymic Stage		Functional Severity Stage			
		I	II	III	IV
Asymptomatic & Peripheral	(1)	A	A	C	D
Symptomatic or Central	(2)	A	B	C	D
Vicinal	(3)	B	B	C	D
Isothoracic	(4)	C	C	C	D
Intrathoracic	(5)	C	C	D	D
CNS, Surface, Bone	(6)	C	C	D	E
Liver/Other	(7)	D	D	D	E

Code Composite Stage

1 = A

2 = B

3 = C

4 = D

5 = E

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